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JUVENILE SCHIZOPHRENIA

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This brief review is preceded by the report of a case of schizophrenia in an African juvenile, a condition which I have not found described in the literature. One of the objects of the paper is to demonstrate that psychiatry is not divorced from general medicine, and to draw attention to the fact that fascinating clinical and research material exists in our mental hospitals.

CASE REPORT

This Zulu lad (K.M.), aged 13 years, was admitted to the Fort Napier Hospital on 6 May 1955. The only abnormal finding on physical examination was a bilateral enlargement of the breasts. On special investigation there was evidence of abnormal liver function tests:

	26 *Jul.* 56	28 *Sep.* 56	4 *Jan.* 57
Serum bilirubin, mg./100 c.c. ..	0·4	0·2	4·6
Serum protein, g./100 c.c. ..	6·2	6·2	5·84
Serum albumin, g./100 c.c. ..	3·0	1·48	—
Serum globulin, g./100 c.c. ..	3·2	—	—
Albumin/globulin ratio ..	0·9/1	0·3/1	—
Alkaline phosphatase, K-A units	20·1	41	53·6
Zinc-sulphate turbidity, units ..	2·0	4·8	4·6
Cephalin-cholesterol flocculation	+	±	−
Thymol turbidity, units	— ..	1·2	—
Serum alpha-1 globulin, g./100 c.c.	— ..	1·02	—
Serum alpha-2 globulin, g./100 c.c.	— ..	1·21	—
Serum beta globulin, g./100 c.c. ..	— ..	1·19	—
Sera gamma globulin, g./100 c.c. ..	— ..	1·30	—

Mentally he was fatuous, fidgety and manneristic; he appeared confused and replied to questions either by grinning or by repeating the question put. His intimate habits were faulty, but some days he would manage to keep his trousers dry and clean. He would bite himself impulsively and throw stones repeatedly, but aimlessly.

The mother of the patient gives the following account: She had 7 children before the birth of K.M. They were all of normal intelligence and free from psychotic signs. Two were drowned, one died as a result of burns, and one died after an illness of 3 days' duration at the age of 1 year. She says that as she had 7 other children she was able to judge the intelligence and behaviour of K.M. to be 'normal' up to the age of 5 years, when he would do the family errands to neighbouring kraals without errors. At the age of 6 years she noticed that K.M. was no longer behaving normally. It was not possible to converse rationally with him. He would eat the tapeworm segments which he had passed. For 2-3 years before his admission to Fort Napier Hospital she tried various witch-doctors.

The patient was breast-fed until he was 2 years old. She says that the feeding of each of her children was accompanied by swollen breasts, which used to discharge and were painful. She also has a large colloid goitre, which she states she has had 'since birth'.

Her husband was a migrant labourer and used to send her £6 a month, but he died at the time of K.M.'s birth and then she had to depend on charity, which was never generous.

Treatment. He received a course of Ectonus electroplexy (16 treatments) during the period 23 May—24 June 1955, and after the electrical treatment he was given a course of vitamin B_{12} injections.

Although his response to treatment was on the whole not satisfactory, there was evidence of a degree of improvement. Eighteen months after the course of electrical treatment he was still manneristic, fatuous and withdrawn, but his replies to questions were relevant, his habits were consistently correct, and he worked well under supervision.

DISCUSSION

Sackler *et al.*[1] report on the high incidence of thyroid dysfunction in the mothers of 19 juvenile schizophrenic patients. It is well known that liver disease may cause mental symptoms, that the liver may suffer damage from malnutrition at an early age, and that such damage can even be congenitally acquired. These findings are described by Jeliffe,[2] who refers to liver biopsies on apparently healthy Yoruba babies in the first week of life. The biopsies showed marked fatty change. Laurie,[3] in a personal communication, informed me that autopsies on newborn Africans not infrequently reveal fatty change in the livers of these infants, often of marked degree. Gillman and Gillman[4] and Williams[5] stress the fact that diet plays an important part in the metabolism and the consequent development of the individual. Gillman and Gillman also suggest that psychological factors can influence metabolism: 'In man too, in whom so much in life has emotional content, the repercussions on metabolism of many actions can be enormous.' When our African patient showed no response to electroplexy, I was encouraged to try vitamin B_{12} on the strength of (*a*) a description of its apparent ability to cause regression in neuroblastomata,[6] and (*b*) a hypothesis that where neural structures are damaged it causes 'an occasional direct stimulation of functions of the elements not destroyed'.[7] Sargent and Slater[8] comment on the rapid growth of our knowledge on diet and vitamins in relation to mental disease and consider that we are not yet in a position to be dogmatic on the subject.

I did not use largactil on our African patient for fear of adding another burden to what might be a damaged liver. Mayer,[9] however, claims that 'patients with hepatic disease showed an increased responsiveness to the drug and were particularly prone to exhibit sedation, probably as a result of the decreased rate of destruction of the drug by the liver.'

Electroplexy

Some authors believe that electroplexy has a definite place in the treatment of schizophrenia, but others consider it to be a mere auxilliary of insulin coma therapy, or else a maintenance treatment for the chronic patient. Clardy and Rumpf[10] treated 9 schizophrenic patients under the age of 12 with electroplexy. The effect was only temporary in all these cases. Considerable work has been done at

Bellevue Hospital, New York, with electroplexy in children but I do not have their results. Bender[11] describes this form of treatment in a boy aged 34 months, with an increased rate of improvement, and in other patients[12] who received electroplexy in their 2nd, 3rd and 4th years, with gradual improvement afterwards—in some cases 2-3 years later—but she makes no dogmatic claim that this procedure (nor the intensive psychotherapy which some of these children had as well) was the critical factor 'in the child's improved maturation and toleration of his primary schizophrenic disorder'.

Differential Diagnosis

Diagnostic recognition will be especially difficult when the schizophrenic reaction occurs in a child with an introverted and solitary disposition. Among the conditions to be excluded from the diagnosis are:

(1) The normal child,[13] (2) severe hysterical reactions, (3) low-grade mental defect, which in turn must be differentiated from (*a*) schizophrenic amentia, in which condition the amentia is secondary to the dementia praecox[14] and (*b*) pfropfschizophrenia, where schizophrenia develops in a defective,[14] (4) juvenile general paresis, (5) trauma, (6) encephalitis, (7) disseminated sclerosis, (8) infestation of the brain with (*a*) larval forms of *Taenia solium*,[15] (*b*) coernurus cerebralis,[16] (*c*) bilharzia[17] (*d*) ascaris,[17] and (*e*) malaria, (9) hypothyroidism and hyperthyroidism.[18]

Incidence

Because of the heterogeneity of schizophrenia, various figures are quoted for juvenile schizophrenia:

1. Mayer-Gross *et al.*[13] make the following comments. 'Schizophrenia is probably no more frequent than manic-depressive psychosis in children, but the diagnosis is more often made. Recently almost all psychotic conditions seen before puberty have been called schizophrenic . . . The real incidence of schizophrenia in childhood is very low indeed. Many experienced psychiatrists have never seen a schizophrenic patient younger than 11 or so.'

2. Bradley, quoted by Bellak,[19] considers the frequency of dementia praecox in children to be about 1% of dementia praecox of all ages.

3. Bender[20] says that of 6,500 children up to 13 years of age seen by psychiatrists of Bellevue Hospital, New York, from 1934 to 1951, 626 were diagnosed as schizophrenic. Of these, 5% were not more than 5 years old. This figure is apparently based on a selected population and, therefore, does not indicate the occurrence of the illness in the general population.

4. Tredgold[14] considers the proportion of schizophrenic aments to be probably about 1% of all defectives.

5. In an annotation[21] in the *British Medical Journal* it is suggested that psychoses in children are not as rare as has been thought. Puzzling nomenclature is considered to be an important factor contributing toward this state of affairs.

6. A point worthy of mention is that schizophrenia in the African would appear to be of an amorphous form. This view is supported by Carothers[17] and Smartt.[22]

7. Kallman[23] states that 'in the main groups of childhood behaviour disorders (including childhood schizophrenia) and adult psychoses, the male sex is grossly over-represented before adulthood and under-represented throughout adulthood. He gives the proportions for schizophrenic males over 14 and under 14 as 46·1% and 74·6% respectively. He quotes Bradley, Dispert, Richards, and others who attributed the preponderance of males to females in childhood schizophrenia to the relatively protected position of the female in the American culture, but he (Kallman) points out weaknesses in the theory and can offer no biological explanation for this sex variation.

Prognosis

The prognosis in schizophrenia is variable and depends on a multiplicity of factors, such as duration of illness, age, mode of onset (whether sudden or gradual), type of schizophrenia, psychotic symptoms, heredity, bodily build, and (perhaps) sex. The prepsychotic personality and precipitating factors are also important. The prognosis of childhood schizophrenia is generally considered poor. Bellak,[19] quoting Loy, states that a review from the literature of different countries revealed that of 50 cases 66% showed no improvement, 19% improved but relapsed later and only 14·4% showed lasting improvement. Mayer-Gross *et al.*[13] give a figure of 1 out of 14 prepubertal schizophrenics making a good adjustment. Bender[12] says that follow-up studies have confirmed that childhood schizophrenia forecasts adolescent and adult schizophrenia, but she goes on to say that the prognosis is much better than formerly held.

SUMMARY

This is the case report of an African child with gynaecomastia and abnormal liver-function tests, who presented with a schizophrenic reaction that commenced at 6 years of age. The mother has a large colloid goitre. The treatment, differential diagnosis, incidence, and prognosis of juvenile schizophrenia are discussed.

I should like to thank Prof. I. R. Vermooten, formerly Commissioner for Mental Hygiene, for permission to publish this paper; Dr. W. Laurie, Senior Pathologist, Edendale Hospital, Pietermaritzburg, for valuable assistance; and Dr. M. Ginsburg, Physician Superintendent, Sterkfontein Hospital, Krugersdorp, for encouragement.

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VAN DIE REDAKSIE : EDITORIAL

PRIMÊRE HIPO-ALDOSTERONISME

Na die beskrywing deur Conn[1] in 1955 van 'n kenmerkende sindroom veroorsaak deur primêre hipersekresie van aldosteroon, het daar uitgebreide belangstelling in en navorsing oor dié aspek van die sout- en waterhuishouding, gereël deur die bynierskorshormoon, gevolg. Die belangstelling was hoofsaaklik gerig op primêre en sekondêre hiperaldosteronisme. Die sindroom van primêre hiperaldosteronisme is vandag goed bekend. Ook word die belangrike rol wat die bynier (sekondêr) in verskillende patologiese toestande speel, byvoorbeeld in hartversaking, nefrose, en in lewersirrose, besef. Van primêre hipo-aldosteronisme is egter min bekend. Conn[4] beweer dat die toestand van primêre bynieronvermoë om voldoende aldosteroon uit te skei in die teenwoordigheid van vermoë om voldoende ander bynierhormone uit te skei, nog nie beskryf is nie. Hy beweer egter dat die moontlikheid wel bestaan. Gedurende 1957 beskryf Hudson *et al.*[2] 'n geval met volledige hartblok waar 'n hartstilstand deur spontane aanvalle van hiperkalemie teweeggebring is. Die bevindings, nadat uitgebreide studies in verband met nierfunksie en die ander hormoon-uitskeidingsprodukte van die bynier gedoen is, het daarop gedui dat die hiperkalemie deur 'n alleenstaande gebrek van aldosteroon-uitskeiding veroorsaak is. Dié bevindings is verder gestaaf deur die bevinding van baie lae aldosteroon-waardes in die urine voor en na soutbeperking. Die gebrek in kaliumuitskeiding was die duidelikste waar die pasiënt op 'n lae natrium-dieet geplaas is. Genoemde skrywers doen aan die hand dat die geval moontlik 'n voorbeeld van suiwer hipo-aldosteronisme is. Dit is egter nie vasgestel of die primêre fout in die bynierskors is, of in 'n 'n tot-hede-toe-onbekende regulerende meganisme buite die bynier, geleë is nie.

Uit Swede word gedurende 1958 deur Skanse en Hökfelt[3] berig gedoen van 'n geval gekenmerk deur floutes, swakheid, en hipotensie, met die verdere bevindings van geen meetbare hoeveelhede aldosteroon in die urine nie. Geen simptome en tekens van ander bynierskorshormoon-gebrek kon aangetoon word nie. Verder kon geen bewys van 'n primêre fout met die niere wat verantwoordelik gehou kon word vir die toestand, aangetoon word nie. Die skrywers beskou dit as 'n verdere geval van primêre hipo-aldosteronisme, maar was nie by magte om af te lei of die stofwisselingsfout *in* die bynier of *buite* die bynier geleë was nie.

Dit blyk duidelik uit die beskrywings dat die twee gevalle verskil wat betref hul simptomatologie, maar dat hulle nogtans een gemeenskaplike faktor, te wete, verminderde meetbare uitskeiding van aldosteroon in die urine, het. Skanse en Hökfelt[3] soek, as moontlike verklaring vir die teenstrydigheid in die simptomatologie, die teenwoordigheid van primêre hartpatologie met versaking in die geval van Hudson, maar beweer ook dat die hartpatologie die gevolg van langdurige hipo-aldosteronisme kon gewees het.

Op grond van die huidige metodes van ondersoek van nier- en bynierfunksie skyn dit asof daar duidelike bewys gelewer is van 'n kliniese toestand wat veroorsaak word deur 'n primêre gebrek aan die uitskeiding van aldosteroon. Die antitese van hiperaldosteronisme is gevind, en 'n nuwe veld van denke en ondersoek, veral in gevalle wat voordoen met onverklaarde hipotensie, hiponatremie en hiperkalemie, is nou oopgestel. Elders in hierdie uitgawe publiseer ons 'n artikel oor '*Chemical and Clinical Endocrinology of Aldosterone*' waarin 'n oorsig gegee word van die meeste probleme in hierdie verband.

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ROAD SAFETY

Grave concern for the serious and far-reaching medical, social, and broader human implications of the present unsatisfactory traffic conditions in our country has recently been expressed both in the general and in the medical press. In his recent valedictory presidential address, Mr. J. G. du Toit,[1] for instance, drew attention to the disease of road accidents; and in last week's *Journal*[2] a letter from Mr. G. T. du Toit was published in which certain practical measures that are being adopted here and elsewhere to ensure greater safety on the roads were highlighted, and in which he discussed the value of such measures as the use of safety belts in motor-cars.

It is not our purpose to discuss again the statistical details of road accidents in our country. Those who are interested in these details will find them in Mr. du Toit's address, to which we have just referred, as well as in the articles regularly published in the daily press and in the records of the National Road Safety Organization which since 1949, has rendered invaluable services towards road safety in this country. What we propose to do is to define the general principles for a broad frontal attack on this problem and to stress the urgent need for an approach of this nature at the present time.

In the first place we must point out that this problem has now assumed such proportions that the only hope we have of handling it with any degree of success, is to adopt a truly national plan of action. Our first need is for a central planning and advisory council comprising senior representatives of the Government and augmented by members of the local and central transport and traffic departments,

members of the National Road Safety Organization, members of the medical profession, and representatives of the general public.

Matters of principle with which the advisory council will have to deal will include: problems of town and street planning and the building of roads; traffic regulations such as speed limits for all kinds of vehicles, including ordinary and power-driven bicycles, motor-cycles, motor-scooters, light and heavy motor cars (especially the large modern cars which are capable of developing a degree of horse-power greatly in excess of any driver's requirements), lorries and buses; the establishment of a national traffic corps which should operate on all the main roads in the country—as an extension of the services of local traffic officers; the standardization of the procedures of registration and re-registration of all drivers; the formulation and implementation of comprehensive schemes of education in the principles of road safety for schoolchildren and adults; sustained imaginative publicity; and systematic research into all the important human and technical facets of the problem of road safety.

Secondly, it is our firm conviction that effective action on the individual level is as indispensable as the measures carried out on a national level. We should be lulled into a false and dangerous sense of security if we were to believe that a national traffic organization would exempt us, as individuals, from all responsibility in this vital matter. Indeed, in this as in all other problems of community life, we have to rely ultimately on the individual conscience and sense of responsibility in every person if we hope to achieve a stable and satisfactory way of life.

Some of the aspects of this problem which may be regarded as matters of personal responsibility, are: the continual cultivation and stimulation of a social and road conscience and of courtesy and goodwill; and a realization of the imminent dangers of the use of alcohol by drivers, of speeding and the many forms of immature behaviour of motorists, who feel the need for bolstering their egos by their flamboyant driving leading so often to fatal accidents.

In the matter of our complicated modern traffic system, as in all other matters touching on our community life, we, as responsible and civilized people, will have to realize the urgent need for cooperative action as individuals, groups and organizations, in negotiating our way through the world with a greater measure of safety and security for all.

1. du Toit, J. G. (1959): S. Afr. Med. J., 33, 296.
2. Correspondence (1959): *Ibid.*, 33, 447.

CHEMICAL AND CLINICAL ENDOCRINOLOGY OF ALDOSTERONE*

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It is less than 30 years ago that the first extracts of the adrenal cortex were used experimentally to prolong life in adrenalectomized animals[1] and purified extracts ('cortin') were employed in cases of Addison's disease. While the use of 'cortin' and subsequently desoxycorticosterone (synthesized in 1937) was accepted substitution therapy, it was well established that the 'amorphous fraction' of the adrenal extract or whole adrenal preparations had more potent action on organic and mineral metabolism in adrenal insufficiency than crystalline preparations. Further, when cortisone and cortisol became available 10 years ago, it was soon evident that doses adequate to normalize organic metabolism lacked capacity to maintain normal salt metabolism.

Discovery of the Salt-regulating Hormone of the Adrenal Cortex

Recent developments in biochemical techniques, particularly chromatography, have led to the isolation of a considerable number of discrete steroids (corticoids, androgens, progestogens and oestrogens) from the adrenal glands. The division into gluco- and mineralo-corticoids, particularly stressed by Selye, is really only relative, since each steroid has effects on organic and salt metabolism in variable degree. Examination of adrenal-vein blood and effluents from perfused glands indicated that the major active secretion in man is cortisol, with lesser amounts of cortisone and corticosterone; in other mammals, corticosterone formed a greater proportion of the secreted corticoids.[2] Consideration of desoxycorticosterone as a hormone has been controversial, since for many years after its discovery this steroid could not be detected in adrenal-vein samples. Further, despite recent identification of desoxycorticosterone in adrenal-vein blood and perfusates,[3] the amounts do not appear to be adequate for significant biological action. At best, desoxycorticosterone only resembles in part the action of a natural electrolyte-regulating adrenal hormone.[4]

Isolation of aldosterone. The impetus for the isolation and characterization of a natural salt-retaining hormone was provided by the work, starting in 1950, of Luetscher and his associates.[5,6] They found high titres of a sodium-retaining substance in the urine of patients with oedema, by assay of urinary extracts injected into adrenalectomized animals (it is a curiosity of nature that the best source of aldosterone at present is the urine of nephrotics, whose daily excretion may be 0·05-0·2 mg.). Subsequently, the Simpson and Tait group from Middlesex Hospital, using chromatographic methods for steroid separation just published by Bush[7] in England and Zaffaroni[8] in the United States, and increasing the sensitivity of the bio-assay test by using flame photometric and isotopic measurement of the urinary Na/K ratio, isolated a highly potent, pure salt-retaining hormone ('electrocortin') from the 'amorphous fraction', adrenal-vein blood and urine in 1952.[9-11] This constituted adequate evidence that 'electrocortin' is a normal secretory product of the adrenal gland; it is now generally accepted that it accounts for about 75% of the salt-regulating activity of the adrenal gland.

The *chemical constitution* of the salt-retaining hormone gave rise to much speculation, until finally the Middlesex and Basle workers in collaboration[12] determined its formula in 1954 (Fig. 1). From the figure it is seen that crystalline

* Revision of talk to the S.A.I.M.R. Scientific Club, Johannesburg, 12 May 1958.

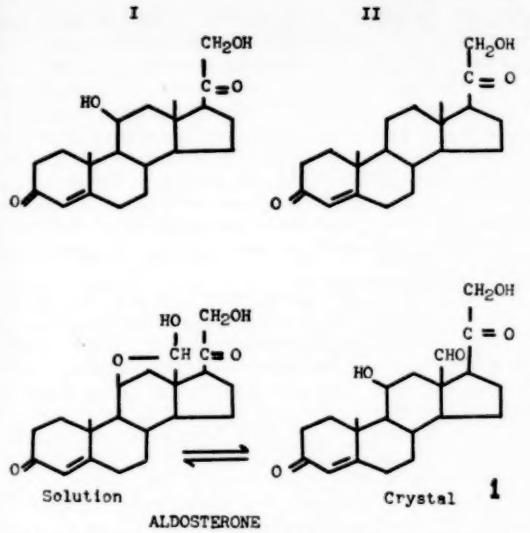

Fig. 1. Chemical structure of aldosterone. I—Corticosterone. II—Desoxycorticosterone. Aldosterone (crystalline) — note 18-aldehyde group. Aldosterone (in solution)—note 11-18 hemiacetal group.

aldosterone has the same basic structure as corticosterone and desoxycorticosterone and is, in fact, the 18-aldehyde of corticosterone (whence its name). Subsequently, independent confirmation came from various sources and Luetscher's salt-retaining substance in nephrotic urines[13] was shown to be aldosterone. The structure of aldosterone is unique among biological steroids in that it (*a*) has an 18-group, and (*b*) exists largely in solution in an hemiacetal form. This may account for its great biological activity, since recently the acetal preparations of cortisol and prednisolone have been shown to have many times the activity of the parent substances.[14]

Biosynthesis of Aldosterone

The demonstration by the Tait group[15] that incubation of beef adrenal-gland capsules gave the highest yield of aldosterone has located the site of formation in the zona glomerulosa. Decapsulated glands yielded little or no aldosterone, nor did incubation of separated fasciculata-reticularis zones. This observation has been confirmed for the rat adrenal,[16] and Conn's suggestion that the adenoma of the first described case of Conn's disease[17] arose in the zona fasciculata would appear to be in error. The present source of crystalline aldosterone is by isolation from beef or hog adrenal (0·05-0·1 mg./kg. in beef and up to 10 times as much in hog adrenal glands). Recently, the chemical synthesis of aldosterone by different processes has been announced,[18,19] and this will, it is hoped, solve the supply problem in therapy and investigation.

Evidence is accumulating that aldosterone is also formed in the placenta.[20]

Nature of adrenal precursors of aldosterone. Incubation of adrenal tissue from various animals with different steroids has resulted in somewhat different findings, probably related to slight variations in experimental conditions. However, in essence, progesterone, desoxycorticosterone and corticosterone (and only these steroids) all increase aldosterone production *in vitro*. In the conversion of cholesterol to adrenal steroids, progesterone is an essential intermediate. This keystone steroid leads to the formation of adrenal androgens, oestrogens and cortisol (with cortisone as its by-product) by one major metabolic pathway, and desoxycorticosterone, with corticosterone and aldosterone derived from it (Fig. 1) by a second major conversion.

Metabolism of Aldosterone

Knowledge of the metabolism of aldosterone has been considerably extended in the past year by the administration of ^{14}C-steroids and more recently of 16-^{3}H progesterone (with much higher specific activity) in animal and human experiments. Human secretion of aldosterone may be put at 0·2 mg./day on normal salt and 0·8 mg./day on low salt intake (by comparison, normal secretion of cortisol is 25 mg./day). Blood concentration is probably 0·05 microgram % (compare cortisol, 10 microgram %). At present the only feasible blood method is that of isotopic dilution, with addition of radioactive aldosterone *in vitro*.

A further difficulty in the study of aldosterone metabolism is that urinary excretion ranges up to 0·01 mg./day, depending on the variation in normal salt intake. Since this represents only some 5% of the daily secretion, and other aldosterone metabolites in the urine amount to less than 20%, correlation of urinary aldosterone content and adrenal secretion may be misleading. Nevertheless, urinary aldosterone estimation is at the moment the only feasible method of assessing adrenal secretion of salt-regulating hormone. Most laboratories are abandoning the bio-assay technique for chromatographic methods[21-23] (the author had the opportunity of developing a modification of a method[21] in the Department of Chemical Pathology, King's College Hospital Medical School, London). For any degree of accuracy, the methods are complicated and tedious, require great attention to technical detail, and must perforce remain in the sphere of special investigation.

Function of Aldosterone

Life maintenance. Doses of 0·001-0·002 mg./kg./day maintain life and electrolyte balance in adrenalectomized animals and Addisonian patients. Higher doses may cause some salt and water retention, but not when cortisol is given concurrently.

Electrolyte effects. Aldosterone influences the distribution of sodium and potassium (and magnesium) between the intra- and extracellular compartments by increasing the rate of exchange between cell potassium and magnesium and extracellular sodium—thus decreasing sodium and increasing potassium and magnesium in saliva, sweat, urine, etc. Quantitatively, its action on urinary composition is of particular importance, since it enhances the exchange of sodium in the tubular fluid for cellular potassium in the distal convoluted tubule (Fig. 2). Aldosterone has some 250 times the sodium-retaining potency of cortisone or cortisol for equivalent dose and 30 times that of desoxycorticosterone, and is approximately equivalent to the synthetic 9α-fluorohydrocortisone. Aldosterone has 5 times the activity of desoxycorticosterone in enhancing potassium excretion.

Effects on water excretion. The end-result is dependent on the interplay of steroid action on sodium excretion, glomerular filtration rate and tubular reabsorption of water,

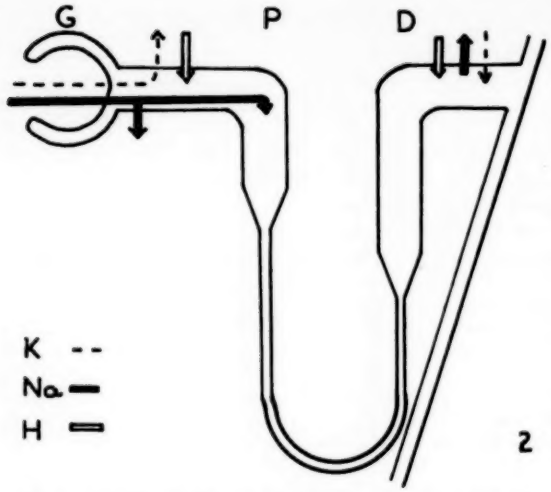

Fig. 2. Action of mineralocorticoids on the renal tubule. G—Glomerular filtrate: 600-800 mEq. K, 18,000-25,000 mEq. Na. P—Proximal tubule: all K reabsorbed, 85-90% Na reabsorbed. D—Distal tubule: Na—K and Na—H exchange modified by aldosterone.

the latter either by local action or conditioned by steroid effect on the secretion of antidiuretic hormone (ADH)—thus adrenal corticoids may be diuretic or antidiuretic according to the steroid, the dose and the particular physiological or pathological conditions operating at the time. For example, while aldosterone has been reported to have no direct effect on water excretion nor to repair the inability of the adrenalectomized dog or Addisonian patient to excrete a water load, other studies have indicated that this steroid can increase glomerular filtration and produce diuresis in adrenalectomized rats.[4]

The *glucocorticoid effects* of aldosterone are as follows:

(*a*) Carbohydrate metabolism: Aldosterone deposits liver glycogen, having 1/4th - 1/3rd the activity of cortisone and 25 times that of desoxycorticosterone.

(*b*) Stress: Aldosterone is more effective than cortisone or desoxycorticosterone in protecting against cold stress.[24] The excretion of aldosterone is increased in heat stress.[25]

(*c*) Connective tissue: Aldosterone has no anti-inflammatory or allergic action, nor does it inhibit granuloma formation.

(*d*) ACTH release: Unlike cortisone or cortisol, aldosterone does not suppress endogenous pituitary adrenocorticotropin.

Blood pressure. Aldosterone produces none of the pathological changes seen with desoxycorticosterone of equal sodium-retaining potency. However, high dosage combined with high salt loading has produced hypertension in rats, with renal and vascular changes of mild degree.[4]

Control of Aldosterone Secretion

The stimulus to aldosterone secretion arises as a hypothalamic neuro-hormone, postulated to result from alterations in effective blood volume, which acts on hypothetical volume receptors[26] (? sited in lungs, heart atria,[27] arterial tree, brain). The response (1) shows a time delay of several hours and (2) appears to react more to rapid blood volume changes than slow; and (3) effects on renal electrolyte excretion follow several hours after alterations in aldosterone secretion.

The neuro-humoral transmitter must be regarded as separate from ACTH action, since aldosterone continues to be secreted at about 50% of normal rate after hypophysectomy and continues virtually unaltered after ACTH administration. The administration of ACTH in therapy or to normal individuals produces a small increase of aldosterone secretion. Similarly, suppression of endogenous corticotropin with large doses of cortisone alters aldosterone secretion to a slight degree.

However, by the use of purified ACTH fractions, Farrell *et al.*[28] has shown that A-corticotropin, comprising about 10% of his ACTH preparations, had 20 times the aldosterone-stimulating activity compared with B-corticotropin, so that variation in the amounts of the different components in therapeutic preparations or actually secreted by the pituitary gland will account for variation reported by different investigators. In any event, it is apparent that the secretion of aldosterone is not under complete and direct control by ACTH. The complexity of the problem is indicated by the fact that injection of growth hormone in animals and man appreciably increases the secretion of aldosterone.

If the effective blood volume is the stimulus to the diencephalon, then the following sequence of reactions may

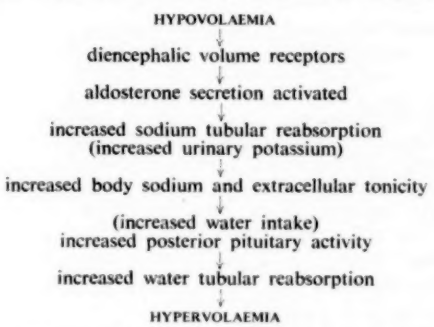

Fig. 3. Homeostatic regulation of extracellular fluid. Aldosterone controls body sodium (slow action). ADH controls body water (rapid action).

be postulated to occur as a dual 'feed-back' mechanism (Fig. 3). Allied to this homeostatic regulation of body fluid, consideration must be given to the possibility that changes in blood volume or flow may alter the flow through the liver and so alter the degree of hepatic inactivation of aldosterone and ADH.

The stimulus continues to act if the compensating mechanisms cannot function. For example, large amounts of aldosterone are present in the urine of cirrhotics with ascites, since the retained fluid fails to inactivate the retention mechanism because the fluid becomes progressively segregated in a non-circulating compartment.

Increased secretion of aldosterone (indicated by elevated urinary aldosterone) occurs (1) during deprivation or depletion of sodium and (2) during addition of potassium. Apparently the potassium loading must cause sodium loss to produce the increase in secretion. Since haemorrhage, sweating, diamox diuresis etc. all increase aldosterone

secretion, the common factor is sodium and water loss, i.e. loss of body fluid.[29] Conversely, sodium addition and, to a lesser extent, potassium depletion depresses aldosterone secretion.

While the secretion of aldosterone is subservient mainly to the requirements of body-fluid volume control, other factors, e.g. sodium excretion,[6] renal haemodynamics, concentration of tissue electrolytes etc. are probably also involved.

CLINICAL ALDOSTERONISM

In retrospect, it is apparent that aldosterone dysfunction was responsible for many of the signs and symptoms in adrenal insufficiency; yet, on the other hand, Cushing's syndrome shows no clear signs of aldosterone hyperfunction. This is due to the fact that other adrenocortical hormones have effects on mineral metabolism; for example, the daily secretion of cortisol is about 100 times that of aldosterone, so that although the electrolyte action of cortisol on an equivalent weight basis is small compared with aldosterone, its total effect is quite considerable, apart from qualitative differences in its electrolyte effects. *The relative proportions of secretion and inactivation of corticosterone, cortisol and aldosterone control the net effect of the adrenal cortex on electrolyte metabolism.*

Syndromes of Primary Hyperaldosteronism

1. *Aldosteroma* (Conn's Disease)

Excessive wastage of potassium by the kidneys, with severe and persistent hypokalaemia leading to periodic paralysis, had for some years been attributed to a primary renal lesion, viz. potassium-losing nephritis.[30-33] However, Conn, finding low Na/K ratios in excretory body fluids in a similar case, together with a sodium-retaining factor and no increase in 17-hydroxycorticoids in the urine, concluded (October 1954) that the excess excretion of electrolytes might be due to overaction of the then newly discovered hormone, aldosterone.[17] Exploration revealed an adrenal adenoma, removal of which cured the disorder.[34,35] Once the cause had been found, several cases of 'potassium-losing nephritis' were identified as Conn's disease in retrospect, adrenocortical adenomata being found at operation or *post mortem* and indicating clearly that the patients had been suffering from primary aldosteronism.

To date, some 35 cases are recorded in the literature and others are known to the author. They occur mainly in adults. An interesting feature of the first 15 cases described is that symptoms had been present for long periods (½ - 15 years) and that the patients had been admitted on several occasions before the correct diagnosis was made. The clarification of the aetiology and symptomatology is a considerable advance for this essentially remediable condition.

Clinical features. The characteristic signs in the fully developed case may be classified as follows:

(*a*) Severe electrolyte disturbances—hypokalaemic, hypochloraemic alkalosis, with gross body-potassium depletion; high normal or raised plasma sodium.

(*b*) Attacks of muscular weakness or paralysis, with occasional paraesthesiae or tetany. Despite considerable potassium depletion, most patients are surprisingly well between attacks.

(*c*) Hypertension, moderate to severe. Every case of hypertension with neutral or alkaline urinary pH in a young person should probably have plasma-potassium and bicarbonate estimations and a potassium-repletion test done (followed by steroid studies if required).

(*d*) Widespread impairment of kidney function—polyuria; inability to concentrate urine; low maximum urinary specific gravity resistant to pitressin; alkaline or neutral pH with little response to ammonium-chloride administration; intermittent proteinuria; and reduced clearances. The changes are partly or completely reversed when the potassium deficiency is corrected by removing the adrenal adenoma. Since experimental potassium depletion or deficiency from extrarenal causes leads to similar renal effects, the urinary alterations may be attributed in major degree to potassium deficiency. Once the condition has been present for several years, clear-cell nephrosis and nephrosclerotic changes may supervene, with hypertension and pyelonephritis (potassium-depleted kidneys secreting an alkaline urine are prone to infection). In these cases, recovery of renal function may be incomplete once the tumour has been removed.

(*e*) Endocrine aspect. The reported values for urinary aldosterone in Conn's disease are not impressively increased;[36] they may be at upper normal or slightly raised levels, and are noticeably less than in secondary hyperaldosteronism. The problem arises, how can such levels account for the severe electrolyte and hypertensive disturbances? Undoubtedly a time factor is involved. No urinary aldosterone values are yet available for the early stages in the development of the aldosteroma; once the condition is fully developed, the body-potassium depletion will considerably reduce the secretion of aldosterone from normal adrenal tissue.

Diagnosis of Aldosteroma

In the fully developed case, the combination of history, signs and the assembly of biochemical and radiological (air insufflation to demonstrate adrenal tumour) data are sufficiently clear-cut to make a probable diagnosis fairly certain in the light of current knowledge; however, in the early stages of the condition, the mildness of the symptoms make the diagnosis more uncertain. Early operation is of some importance, since renal changes produced by persistent potassium deficiency eventually become irreversible; however, considerable correction of electrolyte and renal abnormalities can be produced with potassium supplements and a low-sodium diet.

The progressive changes produced by the hormonal disorder and the considerable range of presenting symptoms is well illustrated in 2 case reports by Milne and Muehrcke.[37] The one case was a most severe example with a 12-year history of prolonged hypokalaemic paralytic episodes (up to 21 days in duration) and irreversible renal failure. This patient had been previously diagnosed as 'potassium-losing nephritis';[31] considerable improvement followed the removal of an adenoma.[38,38a] The other subject was asymptomatic except for slight hypertension and an electrocardiogram suggestive of potassium depletion. Renal biopsy was normal, and perirenal air insufflation showed no tumour, but some potassium deficiency with excess urinary loss was found. At operation the smallest adrenal adenoma (1·5 cm.) yet recorded was found. The difficulties in diagnosis presented by this case are also reflected in a report by Crane *et al.*[39] The patient had hypertension with occasional attacks of polydipsia. A left Smithwick sympathectomy was done, and

the left adrenal was seen to be normal at the operation. With no improvement in blood pressure and the finding of transient muscular weakness and hypokalaemia, an adenoma of the right adrenal gland and the right sympathetic chain were removed at a second operation, with disappearance of symptoms. In retrospect, it is evident that removal of the adenoma alone would have cured the disorder.

To date, practically all the reported cases of Conn's disease had had more than one admission before Conn's paper[17] indicated the correct diagnosis. In the first described case from South Africa, Eales and Linder[10] concluded, at the time of her discharge (June 1953) after the first admission, that the patient had renal disease and that activity of a 'DOCA-like' substance was responsible for the hypernatraemic, hypokalaemic alkalosis; after several episodes of muscular weakness, a second admission disclosed no change in electrolyte abnormalities, but the patient remained well provided she took supplemental potassium (September 1954). In October 1955 readmission for air insufflation studies revealed a left adrenal tumour, and the adenoma was successfully removed, with disappearance of symptoms.

Brooks *et al.*[36] and Milne and his collaborators,[37,38,38a] discuss the considerable difficulties encountered in distinguishing between potassium deficiency due to renal tubular or adrenal cortical origin. While renal tubular acidosis is rare in adults and can be identified by hyperchloraemic acidosis with a neutral or acid urine, potassium-losing pyelonephritis etc. are not readily differentiated from aldosteroma with secondary renal changes.

For the *differential diagnosis*, the measurement of urinary aldosterone is complicated, tedious and more difficult to interpret than a study of potassium balance and renal function. Asymptomatic hypokalaemia may be the earliest presenting sign. A repletion test with potassium will indicate the degree of body-potassium depletion, and a continuance of low plasma potassium with excessive urinary potassium loss indicates the resistance of the mineralocorticoid excess to correction of the potassium deficit. In mild cases, potassium loss on a low potassium intake will expose the inadequate renal conservation of potassium; but in a case with definite symptoms such a test would precipitate a severe reaction. Alkalosis and hypochloraemia without obvious cause is suggestive; so is benign hypertension in association with an alkaline urine not due to an active urinary infection. The reduced salivary sodium and increased K/Na ratio are considered valuable evidence by some investigators. However, the author has found that only estimations on pure salivary juice under controlled conditions provide a range of normal values to permit assessment of deviations; this finds confirmation in that examination of reported values from aldosteroma cases shows no clear-cut characteristic values.

Excess urinary potassium, with polyuria somewhat resistant to ADH, and a neutral or slightly alkaline (fresh and negative for bacteria) urine with a slight or moderate response to NH_4Cl administration, is evidence of renal changes secondary to the steroid-induced potassium deficiency.

The ultimate diagnosis rests on surgical procedures—renal biopsy, perirenal air insufflation to outline the adrenal gland for radiological examination, and operation by the abdominal route so that both adrenal glands can be examined. In the majority of aldosteromas reported to date, only operation or post-mortem provided certain diagnosis.

2. *Variants of Conn's Disease*

Oedema is not a feature in Conn's disease. However, cases have been reported with oedema and the classical signs described by Conn, and in which, on removal of an adrenal adenoma, the oedema, electrolyte abnormalities and hypertension[41] disappeared. The possibility that other sodium-retaining hormones with qualitatively different effects are secreted by the adrenal cortex requires investigation in such instances.

Several clinicians have reported the occurrence of mild diabetes mellitus associated with proven aldosteromas.[42,43] The glucocorticoid activity of aldosterone is relatively slight, and whether one is dealing with a random association or with diabetes mellitus caused by adrenal steroid (or steroid glucosuria) must await further investigation and reports in other cases.

3. *Mineralocorticoid Excess and Mixed Syndromes*

Apart from localized adenomas of the adrenal (aldosteromas), hyperplasia of the adrenal cortex[32,44-46] and primary[36,47] and secondary[48] carcinoma produce symptoms almost identical with those described by Conn.[17,34,35] *Cases with proved aldosteromas should be called Conn's disease, and other primary adrenal cases with no obvious alteration in glucocorticoid function would be classified as Conn's syndrome.*

The reported cases of hyperplasia of the adrenal cortex leading to Conn's syndrome have occurred almost entirely in children, with a decrease or disappearance of symptoms on partial or total adrenalectomy. Cerebral disturbances[44,46] (hyperpyrexia, convulsions), presumably resulting from excessive hypothalamic stimuli to the adrenal cortex, are considered causative in 2 cases. The rates of secretion of aldosterone and of cortisol can be differentially affected by experimental brain-stem lesions in animals.[49] The relationship between these two cases and the condition of cerebral hypernatraemia and the secondary hyperaldosteronism of idiopathic oedema (discussed below) is obscure at the moment.

While it is noteworthy that none of the described cases of Conn's disease and syndrome have the usual signs of Cushing's syndrome, it is probable that pure aldosteromas or conditions of specific hypersecretion of aldosterone are rare. Tumours or hyperplasia of the adrenal cortex may involve the secretion of aldosterone, corticosterone, cortisol and other adrenocortical hormones in varying degree. This would alter the amount and proportion of sodium retained and potassium excreted and thus the total mineralocorticoid effect. Further, mixed syndromes of mineralo- and glucocorticoid hyperfunction are being recognized. For example, cases of Cushing's syndrome frequently show decreased plasma and body potassium and, where such cases have been examined, the urinary adrenocortical hormones indicate normal or subnormal aldosterone with increased cortisol and corticosterone.[50] Cases of salt-losing adrenogenital syndrome exhibit normal urinary aldosterone values;[51,52] although the synthesis of cortisol has been shown to be defective, with deviation of steroid metabolism to produce excessive amounts of urinary pregnanetriol, a theoretical salt-losing hormone is also considered to be a possible cause of the sodium loss.

Secondary Hyperaldosteronism

In a wide range of conditions, urinary aldosterone excretion increases as a result of abnormalities situated outside the adrenal gland, which responds in a normal manner to the stimuli. The most notable increases occur in conditions of oedema, where the secretion of other adrenocorticoids may be virtually normal. The considerable electrolyte disturbances, with little or no oedema and moderate increase in urinary aldosterone, of the fully developed primary disease contrast sharply with the preponderant fluid disturbances and greater aldosterone output in oedematous conditions. While the volume-control theory (Fig. 3) fits many of the observations in secondary hyperaldosteronism, some investigators are not prepared to accept it as valid; e.g. Conn states, 'Precise physiological or biochemical stimuli for secondary aldosteronism are unknown'.

1. *Oedema and Aldosterone*

The triad of oedema, sodium retention and elevated urinary aldosterone is only found in severe forms of congestive heart failure, in liver cirrhosis with ascites, in nephrosis, in pregnancy with and without toxaemia, and in idiopathic oedema. The *effective* blood volume is low in these cases from other factors (abnormal peripheral and renal haemodynamics, hypoproteinaemia, etc.) and the excess fluid or oedema is segregated in a non-circulating form.

This constitutes a continuing stimulus to an increased production of aldosterone, accentuated since such cases have been salt-restricted or under diuretic therapy for some time. In addition, diminished effective flow through the liver and other organs may decrease the inactivation of aldosterone. Normally, about 5% of secreted aldosterone is excreted in the urine in a biologically active form. The possibility arises that in these conditions more free aldosterone is excreted, with an enhanced effect on sodium reabsorption in the renal tubule.

In *heart disease* the excretion of aldosterone is normal and increases only occur secondarily to the development of cardiac cirrhosis with decreased inactivation of free aldosterone, and oedema as a result of altered peripheral and renal haemodynamics. Therapy aimed at sodium depletion is a further potent stimulus to aldosterone secretion.[53] The disturbance in fluid distribution and sodium metabolism (the reduced effective intravascular volume being the critical factor) fails to inactivate the retention mechanism and reduce aldosterone activity. Sodium and water will be continuously retained until the cycle is broken by rest, digitalis and diuresis. High urinary aldosterone values are associated with intractable oedema and low urinary sodium.

In *liver disease* there is evidence of increased urinary aldosterone. This is due to reduced hepatic inactivation of aldosterone,[54] as a result of which a higher proportion of biologically active hormone circulates and is excreted in the urine. The detection of metabolic products of aldosterone in urine will enable this aspect to be clarified. In hepatic cirrhosis with ascites, the urinary aldosterone rises rapidly with the reaccumulation of ascitic fluid after paracentesis. It is thus probable that the increase in salt-retaining hormone follows the collection of peritoneal fluid precipitated by portal hypertension. The progressive shift of fluid into a segregated compartment leads to further activation of the dual retention mechanism in an attempt to replace sodium and water losses and to prevent hypovolaemia. The failure of the retained sodium and water (because it is not part of the effective blood volume) to reduce aldosterone and antidiuretic hormonal activity results in continuous sodium and water retention by the kidney, unless the cycle is broken by reduction of portal hypertension, restoration of the normal osmotic pressure of the blood, and sodium restriction or diuresis.

In *nephrosis* the aldosterone excretion is greatest during the accumulation of oedema consequent on a decrease in circulating blood volume as a result of hypoproteinaemia. Injection of concentrated human serum albumin or prednisone decreases urinary aldosterone output, but only when diuresis occurs.

In *toxaemia of pregnancy* the urinary aldosterone excretion is considerably elevated. However, the increase in aldosterone output only contributes in part to the sodium and fluid retention, since increases in aldosterone excretion of a greater magnitude occur in normal pregnancy.[55,56] Several operative mechanisms may be suggested: impaired hepatic inactivation of active aldosterone; alteration in the proportion of aldosterone, cortisol, and other hormones secreted by the adrenal; adrenocortical response to maintain effective circulating blood volume in the face of sodium and water loss into maternal and foetal cells; and compensatory response for the sodium-diuretic properties of the increased progesterone output.

Cases have been described in women with emotional stress and tension, of *idiopathic oedema*, in which the only prominent sign was an increased output of aldosterone.[57-59] The condition was unrelated to the menstrual cycle and the oedema subsided on a low-sodium diet. Partial adrenalectomy did not improve the condition in those operated on, nor was any abnormality of the adrenal gland found. A persistent stimulus to the zona glomerulosa of the adrenal cortex from hypothalamic or higher centres is postulated.

A case of massive oedema with sodium retention and no evidence of disease of the heart, liver or kidney illustrates the many complexities in the study of aldosterone function.[60,60a] The patient had had oedema since 1945 attributable to abnormal *capillary permeability to proteins* (high protein content of pleural and oedema fluids). When aldosterone estimations became available, high urinary values were found associated with very low urinary sodium. On exploration, the left adrenal gland containing an adenoma was removed (none of the symptoms and signs of primary hyperaldosteronism were present), with subsequent adequate excretion of sodium and normal urinary aldosterone levels. Six months later, urinary aldosterone again became elevated and only minimal amounts of sodium were being excreted, and a hypertrophied right adrenal gland was then removed. The continued attempts to reduce sodium intake and induce sodium excretion by vigorous diuretic and other therapy led to excessive secretion of aldosterone. The adenoma was functional and the adjacent adrenal tissue contained no aldosterone. With the continuance of the stimulus, the remaining adrenal gland then proceeded to produce excessive amounts of aldosterone. The original cause of oedema persists—when the patient's weight falls below a certain level, symptoms of sodium depletion occur and oedema ensues on sodium administration.

2. *Hyperaldosteronism without Oedema*

Experimentally, aldosterone is less liable to produce *hypertension* than desoxycorticosterone or cortisol with steroid overdosage. Patients with severe benign hypertension have a slight increase of urinary aldosterone,[61] but the increase is moderate and may be related to a deviation in salt intake or metabolism in hypertensives.

Cerebral damage, with the development of chronic hypernatraemia and alkalosis, may result from hypothalamic stimulation of the aldosterone-secreting cells of the adrenal cortex.[62]

In *sodium-losing nephritis* of long standing, the sodium depletion will invoke a secondary hyperaldosteronism;[63] according to the degree and duration of aldosterone hyperactivity, potassium excretion may then increase and renal changes due to potassium deficiency may be superimposed on the original defect.

3. *Temporary Hyperaldosteronism*

Certain conditions produce an episode of increased urinary aldosterone without oedema. Raised levels of urinary aldosterone (and cortisol) with associated retention of sodium and water and increased excretion of potassium occur in the immediate *post-traumatic*[64] and *post-operative*[65] periods. Although the factors involved are necessarily complex, loss of fluid and electrolytes and circulatory inadequacy may be responsible for evoking the adrenal response. Haemorrhage (phlebotomy) will increase urinary aldosterone,[29,66] and so will exposure to high environmental temperatures.[25,67] It is noteworthy that not all stress factors will increase urinary aldosterone (and cortisol); for instance, hard physical exercise has no effect.

In *periodic paralysis* intermittent aldosteronism occurs (Conn *et al.*[68]); both spontaneous and induced paralysis is preceded by large increases in urinary aldosterone and intense sodium retention, followed by excessive loss of potassium. With subsidence of the attack, considerable sodium diuresis occurs, with decrease in urinary aldosterone to normal. Conn concludes that intracellular transfer of sodium precipitates the attack of paralysis and may be prevented or decreased in severity by a low-sodium diet.

HYPO-ALDOSTERONISM

Primary Hypo-aldosteronism

A primary decrease in aldosterone secretion with otherwise unaltered adrenocortical function has been reported.[69,70] The patients had clinical signs attributable to hyperkalaemia (including heart block[69]), and also hyponatraemia and absence of demonstrable urinary aldosterone with normal excretion of other adrenocortical hormones and no evidence of renal dysfunction. As yet, it is not possible to conclude whether the primary error is in the adrenal gland or affects some extra-adrenal regulatory mechanism.

In the hypo-adrenocorticism (decreased aldosterone and cortisol) of Addison's disease or in adrenalectomized subjects, the inadequacy of electrolyte regulation is rapidly demonstrated by any measure that would normally increase the secretion of aldosterone, viz. sodium deprivation or excessive intake of potassium. Neither aldosterone nor cortisone alone is effective in the treatment of adrenal insufficiency. The adrenal crisis that may develop in hypopituitarism shows decreased secretion of cortisol, but urinary aldosterone is usually within normal limits, as would be expected since aldosterone secretion is only slightly influenced by pituitary secretion.

Secondary Hypo-aldosteronism

A transient hypo-aldosteronism occurs after removal of the aldosteroma, until the secretion of aldosterone by the normal adrenal tissue 'revives'. A more persistent decrease in aldosterone excretion occurs during renal insufficiency, oliguria or acidosis; this may be a reflection of potassium retention.

Various drugs decrease the secretion of aldosterone. Amphenone reduces biosynthesis and the release of aldosterone, and of other adrenocortical hormones to a lesser degree.[71] Similarly, the insecticide DDD and pinacolone compounds decrease adrenocortical secretion.[72] Prednisone reduces aldosterone activity, either by hypothalamic action or by competition in the electrolyte reabsorptive process of the renal tubule. Synthetic 'spirolactone' steroids, apparently antagonistic to the action of aldosterone or desoxycorticosterone on renal tubular cells, have recently been developed with potent sodium-diuretic effects in the presence of these two mineralocorticoids.[73,74]

SODIUM-RETAINING AND SODIUM-DIURETIC HORMONES

Comparison of normal secretion rates and the sodium-retaining capacities of adrenocortical hormones brings out the fact that cortisol, secreted at 25 mg./day, has only slightly less total influence on sodium retention than aldosterone (secretion, 0·2 mg./day), while normal circulating desoxycorticosterone contributes little to total electrolyte control. With few exceptions, however, the degree of alteration in aldosterone secretion in disease processes is many times that of other corticoids that have sodium-retaining properties, and aldosterone is thus the mineralocorticoid *par excellence*. However, in some cases of Cushing's syndrome and salt-losing adrenogenital syndrome (described above), the electrolyte disturbance is due to other adrenocorticoids than aldosterone. While synergism or antagonism between the actions of the currently known steroid hormones may provide the correct explanation, it would appear that further investigation of the 'amorphous' fraction of adrenal extracts may prove profitable, since aldosterone may not be the only sodium-retaining hormone of high potency.

Paradoxically, the discovery of aldosterone has set off an intensive search for sodium-diuretic hormones. Under certain conditions (as yet not well defined), both cortisone and cortisol will produce sodium diuresis, possibly due to their action in increasing the glomerular filtration rate. The synthetic 'spirolactone' steroids[73,74] only exert their sodium-diuretic effect in the presence of desoxycorticosterone or aldosterone, and suggest the tantalizing prospect that the adrenal gland may secrete a sodium-diuretic hormone.

While the discovery of aldosterone has solved one fragment of the adrenocortical 'complex' and certain aspects of body-fluid and electrolyte metabolism, it has posed further enigmas for elucidation in the field of adrenal endocrinology.

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COMBINED ENTERIC INFECTION

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Enteric fever is a systemic clinical syndrome which may result from infection with a variety of distinct but related organisms of the salmonella group. In addition to classical typhoid fever, due to *Salmonella typhi*, and paratyphoid fever due to any of the three *S. paratyphi* strains, certain other salmonella strains may produce the picture of enteric infection though the more usual result is an acute gastro-enteritis. Chief amongst these according to Topley and Wilson[1] are *S. cholera-suis*, *S. blegdam*, *S. dublin*, *S. enteritidis var. chaco* and *S. sendai*.

Enteric infection associated with systemic invasion by more than one organism of the salmonella group is by no means common but occurs with sufficient frequency to make the association a recognized entity. It was originally described under the term *fièvre typhoïde intriquée*, by Chantemesse and Grimberg,[2] and the term 'double enteric infection' was introduced by Shaw and MacKay.[3] Several examples of triple infection have however been recorded, and for this reason we have preferred to use the term 'combined enteric infection'. Shaw and MacKay's paper contains an extensive review of the literature and they quote a series of 28 cases of their own occurring in an epidemic outbreak in the Middle East. These infections were due to *S. typhi* (Vi phage type T) and *S. paratyphi B* (Vi phage type 'Dundee').

This brief report concerns a series of 4 cases of combined infection due to *S. typhi* and *S. dublin*. In each case the organisms were isolated from the blood stream. A 5th patient is included where one of the organisms was isolated from the blood and the other from the faeces. However, it is uncertain whether this is a true example of combined infection or whether the patient was a faecal carrier of one type and merely had a superadded single infection with the other organism.

PRESENT SERIES AND BACTERIOLOGICAL METHODS

Whole-blood cultures were performed by the addition of approximately 8·0 ml. of blood to 50 ml. of bile-salt broth. Clot cultures were made by the addition of the residual clot

from 5·0 ml. of blood to 15 ml. of bile-salt broth containing 100 units/ml. of streptokinase, as we have previously described.[4] In both cases subcultures were plated, after incubation at 37·0°C, onto Wilson and Blair's medium. Agglutination reactions were tested by the usual standard methods.

The clinical features of enteric infection are well known and it is not proposed to describe the case histories in any detail. It has previously been suggested that the clinical picture of a combined infection is usually severer than that of a single infection. Shaw and MacKay,[3] however, were unable to observe any specific features in their 28 double-infection patients, as compared with 43 patients suffering from *S. typhi* infection alone.

Of the 4 patients in this series 2 were classified as moderately severe on admission. The 3rd patient had apparently only a mild infection but in spite of this developed a perforation of the gut during the fourth week of illness and died. The 4th patient was admitted with a history suggestive of incomplete abortion and only developed the clinical features of enteric infection after 3 days in hospital. This patient was classified as severe. She also had radiological evidence of tuberculosis of the right upper lobe with cavitation, and died 7 days after admission in spite of chloramphenicol and cortisone therapy.

In cases 1, 2 and 3 both *S. typhi* and *S. dublin* were isolated from the same blood-clot specimens. In case 3 *S. dublin* was also isolated from the urine. In case 4 *S. dublin* was isolated from the blood clot and *S. typhi* from whole blood culture taken at the same time. In the 5th patient referred to, *S. dublin* was present in a blood-clot specimen and *S. typhi* was found in the faeces. In none of the cases was the agglutination reaction of much significance. Patients 1 and 2 responded well to antibiotic therapy.

DISCUSSION

The review of the literature by Shaw and MacKay[3] includes records of 39 isolated cases of double infection and 1 of triple infection as well as 10 epidemic outbreaks of double infection and 4 of triple infection, occurring between the years 1904 and 1951. In all of these the organisms incriminated were *S. typhi* and *S. paratyphi A* and/or *B*. We have been unable to find any previous account of the association of *S. typhi* with a salmonella other than *S. paratyphi*. However, since it is only within recent years that elucidation of the antigenic structure of the salmonella group has been achieved it may be that some of the earlier reports refer in actual fact to salmonellas other than *S. paratyphi*, but which have been designated as such because of lack of the necessary antisera for proper identification.

The mode of infection in the present series of cases was not established. All were admitted to hospital within a matter of 10 days of each other. In addition, 2 further patients were admitted at the same time from whom *S. dublin* alone was isolated from blood-clot specimens. There was no evidence of a possible common source of infection outside the hospital, the patients coming, in fact, from widely scattered areas.

The origin of mixed infections is not definite and it may be that the same mechanism is not involved in each case. The most obvious possibility is that both organisms are ingested at the same time. This is particularly likely to be the case in waterborne epidemics of combined infection. The second possibility is that a carrier of one type of salmonella may acquire an infection with a second salmonella. The resulting infection from the second organism may then in some way allow of re-invasion of the blood stream by the 'carrier' organism. It has previously been shown that *S. typhi* may remain viable within plasma cells in the intestinal lesions and it seems highly probable that similar viable organisms occur in other sites, especially in the spleen and liver. These intracellular organisms appear to acquire a balanced existence with the symptomless carrier host, but it may be that a second infection with another salmonella type precipitates the balance in favour of the parasite with consequent multiplication and re-invasion of the blood stream in sufficient numbers to be detectable by the usual bacteriological procedures.

A third possibility has been put forward in the past, namely that an infecting salmonella strain may undergo mutation to a second salmonella type. The evidence in favour of such spontaneous mutation is not convincing. Recent work on bacterial genetics, particularly with regard to the phenomena of transduction and lysogenic conversion, has shown that bacteriophage isolated from one salmonella strain may produce lysogenization of certain other salmonella strains with the resulting production of a new antigenic component. In the same way it is possible to show experimentally the acquisition of flagellar antigens of *S. typhi-murium* by strains of *S. typhi* so that the resultant cells have the somatic 'O' antigens of *S. typhi* and the flagellar 'H' antigens of *S. typhi-murium*. It is uncertain, however, to what extent transduction phenomena occur in nature. The production of a different salmonella strain in this way (for example, conversion of *S. typhi* to *S. paratyphi A*) is highly unlikely since this would involve the genetic exchange of more than one antigenic factor in addition to alterations of metabolic properties. Normally in the phenomenon of bacterial transduction only one genetic characteristic is transmitted to any one receptor cell.

Several of the earlier reports on combined enteric infections must be treated with reserve since the diagnosis has been made as the result of agglutination tests or else by the demonstration of the organisms in the faeces. There is no doubt that quite unwarranted assumptions are often made from the results of the former test and the demonstration of the organisms in the faeces may merely reflect the carrier state resulting from a past infection.

SUMMARY

Combined enteric infection with two or more salmonella strains is a recognized entity. Four patients, and a possible fifth, with infection due to both *S. typhi* and *S. dublin* are described. Mechanisms for the possible occurrence of such infections are mentioned.

I wish to thank Dr. A. Adnams, Medical Superintendent, Edendale Hospital, Pietermaritzburg, for access to the case notes.

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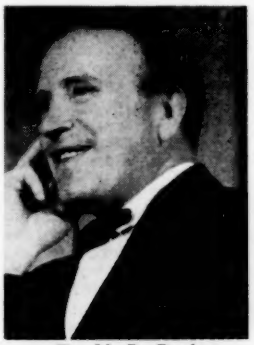
REFLECTIONS ON COS*

N. R. POOLER, M.R.C.P., (LOND.), *President, Natal Coastal Branch, Medical Association of South Africa*, 1958

In the introduction to his work *A History of Europe*, H. A. L. Fisher opens with the words: 'We Europeans are the children of Hellas. Our civilization, which has its roots in the brilliant city life of the eastern Aegean, . . . ' That this is true for the whole of Europe, no one can doubt; but our own profession can pin-point its origin with even more certainty, for our art was born and cradled in the medical school of Cos, under the influence of the greatest of all Greek physicians, Hippocrates. A man very much of his time and place—a characteristic perhaps of all the really great—he lived in the Golden Age of Greece, a contemporary of Plato, Pericles, Socrates and Aristotle.



Dr. N. R. Pooler

Celsus said that Hippocrates divorced medicine from philosophy, but this statement is most misleading. Certainly Hippocrates derided the empty hypothesis, the theory incapable of proof, saying that it belonged to the literature of fiction rather than to medicine. He did not, however, despise philosophy or philosophic reflection. What else could be thought of a man who said, 'The physician who is also a philosopher is like a God'?

Ionian Philosophy

The Hippocratic approach to medicine was evolved from Ionian philosophy—a philosophy which first attempted a commonsense approach to the problems of nature. Until then primitive thought had held sway, ascribing all inexplicable phenomena to the intervention of one or other of a host of deities.

The whole significance of early Ionian thought was that it disregarded these deities and attempted a logical explanation by natural means. How strikingly this is echoed in the Hippocratic writings on the 'Divine disease' (epilepsy): 'It has a natural cause', Hippocrates says, 'just as other diseases have. Men think it divine mainly because they do not understand it, but if they call everything divine which they do not understand, why there would be no end to divine things'.

Here is the authentic Ionian voice pronouncing judgment on a past age—a period of mythological explanation. Hippocrates combined this rational approach to medicine with an insistence on careful observation and accurate record-keeping. Judged by these standards, he can justly claim to have first established the methods of clinical research. His work had great breadth and great vision, for he was the first human ecologist who studied man against his environment 2,000 years before the label 'social medicine' was coined.

The Isle of Cos

To obtain a mental picture of the island of Cos, where Hippocrates was born and learnt his medicine, you must cast your net widely. For if you consult your encyclopaedia or your gazetteer, as in this age of the quiz and crossword puzzle I suspect you do quite frequently, you will only read something like this: 'Cos. A Greek Island in the Aegean Sea. Area 111 sq. miles. Population 20,982. It is famous for its lettuce'. It is, however, unlikely that Hippocrates would have tolerated a medical school establishment in a colony of market gardeners, for he insisted on suitable positions for schools of medicine. I do not think, for instance, that Umbilo Road (the site of the Medical School of the University of Natal) would have appealed to him greatly.

Cos, in fact, was a flourishing centre of Ionian thought and later became a place of poetic and artistic inspiration. Apelles, the greatest of Greek artists, was a Coan. He painted several portraits of Alexander the Great, always in appropriately heroic attitude, hurling thunderbolts or dragging symbolic figures of war at the tail of his chariot. To us, however, Apelles is known by a proverb. He it was, who, when his painting of a sandal was criticized by the local shoemaker, wisecracked, *Ne sutor supra crepidam* (A cobbler should stick to his last).

To this day the wine of Cos is praised by poets. It was a remarkable vintage, prepared with sea-water to give it an authentic tang.

> 'Put out to sea if wine thou would'st make
> Such as is made in Cos when open boat
> May safely launch, advice of pilots take
> And find the deepest bottom, most remote
> From all encroachment of the crumbling shore'.*

And when ready, it was drunk well chilled. For the poet sings:

> 'Summer days are long hot days
> Load up with Asian snow his Coan wine'.†

And with the wine went women, who, moreover, combined their other attributes with a certain usefulness. For 1,000 years before the silkworm arrived in Europe they used the cocoons of certain moths to weave the famous fabrics, known as Coan vestments.

Philitas, the poet of love, made the isle his home. His pituitary was not all that it might have been, and he became so emaciated that he weighed his shoes down with lead to prevent capsizing in gusty weather—a useful endocrine dystrophy to have had in the vicinity of the medical school.

Philitas had two famous pupils, first, the poet Theocritus, whose idyll *Lament for Daphnis* was to be the prototype of Milton's *Lycidas*, Shelley's *Adonais* and Matthew Arnold's *Thyrsis* and, secondly, another pupil closer to our subject, the boy who was to become Ptolemy II of Egypt; for this future potentate was born on Cos.

You must remember that Ptolemy I, his father, was Alexander the Great's bastard half-brother and one of his most successful generals.

On the break-up of the Alexandrine Empire, Ptolemy I gained affluence, not by writing his reminiscences in the modern style, but by grabbing Egypt—the whole of it—an act not unreasonable by the standards of his day. The two Ptolemies between them founded and expanded the great library of Alexandria. It is likely that Ptolemy II, born on Cos, included in the library the writings of his native island and so preserved for us the *Corpus Hippocraticus* as these medical records are often called.

The Corpus

The Corpus itself is a hotch-potch of varying values. Its factual content is poverty stricken by modern standards and even what there is cannot be regarded as strictly original; for the Edwin Smith papyrus recently found in Egypt, and dating from 3,000 B.C., makes it clear that much that we thought to be Hippocratic was known earlier.

It is difficult to understand how the humoral theory of pathology found its way into the Corpus. This farrago of nonsense was the brain-child of that wayward genius, Pythagoras. Pythagoras was an undoubted mathematical genius, but a very peculiar doctor. In the Pythagorian circus was a worker known as Alcmaeon, a man who, with incredible fortitude, dissected dead goats, and this intrepid searcher after knowledge described not only the Eustachian tubes, but also the optic nerves. Such outstanding discoveries allied to Pythagoras' wizardry with figures passed Hippocrates' defences, and into the Corpus the theory went. Even then it might have died a natural death, but for Galen.

Galen

Galen was the evil genius of Hippocratic medicine. By sheer ability he established himself as the leading fashionable physician in Rome in the 2nd century A.D. At that time all the outstanding physicians were still Greek, and Galen, a Greek himself, outstripped them all. A great worker, a gifted observer, a prodigious writer, he had feet of clay. His results were suspect, and he had the mind of a spiv. One can imagine that his togas had built-up

* Valedictory Presidential Address, Durban, 12 February 1959.

* *Sent from Egypt with a Fair Robe of Tissue to a Sicilian Vine-dresser*, 276 B.C., T. S. Moore.

† *Hyali*, James Elroy Flecker.

shoulders and that his villa was next door to the local hippodrome. Galen sold Hippocratic medicine in the market-place, but so great was his influence that he placed Western medicine in a classical straight-jacket, from which it was not released until, in the 17th century, Sydenham of Britain and Boerhaave of Holland tore it free by applying those very principles which Galen had prostituted to constrain it. The theory of the humours dragged on until finally disposed of by the cellular pathologist, Virchow, only 100 years ago.

The most enduring portions of the Corpus are the ethical writings which, taken together, form a considerable part of the whole.

The Influence of Plato

What caused Hippocrates to pay so much attention to the principles of medicine, as distinct from its practice? You will remember that Plato was only 28 when Socrates, his revered teacher, died of the hemlock, and at that time Hippocrates was about 61 years old.

Plato's emotions were stirred to the depth by this tragedy of political bigotry. So deep was the wound, that his description of Socrates' death remains one of the great passages of emotional writing in all literature. You will recall how it ends: 'Such was the end of our friend, whom I may truly call the wisest, the justest, and the best of all men whom I have ever known'.

How likely it is that Plato, leaving Athens in peril of his own life, sought the advice of one who was not only the greatest physician of the day, but also a man renowned for nobility of character.

If the two men met, as well they might have done (Plato mentions Hippocrates with easy familiarity in the *Dialogues*), they must have discussed the just government of man by his fellow men, as well as the safeguards necessary to prevent the repetition of the recent tragedy; and in Hippocrates' mind must have risen the problems of his own profession.

The Learned Professions

In hesitant fashion he drew for us the outline of what we now call a 'learned profession', very much in the image of those ideal forms postulated by Plato in his later philosophical dialogues—a perfect code of behaviour, never to be attained, but never to be forgotten as an ideal towards which we must strive.

Although the term a 'learned profession' is so often used, it is by no means easy to define. The best and most complete definition that I have found postulates the following attributes if an occupation is to be regarded as a true profession.* It must have:

1. *A body of knowledge* held as a common possession which is to be extended by united effort;

2. *An educational process based on this body of knowledge*, in the offering of which the professional group has a recognized responsibility;

3. *A standard of professional qualification* for admission to the professional group, based on character, training and proved competence;

4. *A standard of conduct* based on courtesy, honour and ethics which guides the practitioner in his relations with clients, colleagues and the public;

5. *The formal recognition of status* by one's colleagues and by the state as a basis of good standing; and

6. *An organization of the professional group* devoted to its common advancement and its social duty, rather than to the maintenance of an economic monopoly.

All these attributes are referred to, directly or indirectly, in the *Hippocratic Corpus*. Of all these, there are *three* that at the present time stand out as our greatest responsibilities: (1) Our responsibility for medical education, (2) our standards of conduct, i.e. our ethical code, and (3) the organization of our profession.

1. MEDICAL EDUCATION

Our greatest neglect lies in our lack of interest in medical education. The South African Medical and Dental Council deals only with minimum standards, and such standards can safely be left in its hands. The universities fulfil their obligations to their undergraduates and provide facilities for medical research. And we, who should be vitally interested in those who are to be our colleagues, do nothing in particular and, most of the time, nothing at all.

No one doubts that medical teaching today is becoming less and less a general education, and more and more a scientific training, mainly technical in character. Can medicine ever be solely a scientific technique? Will the day dawn when, provided with the necessary data, a computer will hand out diagnosis, therapy and even prognosis. The question is whether a completely scientific education really fits a man to be a physician. Sir George Pickering, the Regius professor of medicine at Oxford, has recently claimed that it should, and that if it does not, the fault lies with its teachers. Sir Eric James,* high master of Manchester Grammar School, comes nearer the truth when, in speaking to the Manchester Medical Society recently, he said: 'A general education includes the ability to think and talk rationally about *perennial* problems of life and society, and to make judgments of value in a *variety* of fields. Such judgments can arise spontaneously from an education in the humanities. They are less likely to do so from one in science alone'.

It is not without significance that the Selection Board of the Faculty of Medicine of the University of Edinburgh prefers to admit, other things being equal, those students who come from schools famous for their teaching of classical subjects.

The taking of a suitable university degree in arts before commencing the study of medicine, bristles with difficulties. These difficulties are, however, mainly concerned with problems of time and money, both of which can be overcome. At present, the decision to become a doctor has to be taken at far too early an age. A preliminary non-technical course could provide useful time for reflection, and would not by any means be wasted.

Much 'hot air' has been ventilated about the status of the general practitioner. It is my opinion, although I cannot prove it, that in part, at least, this loss of status can be ascribed to the fact that the family doctor is inadequately educated for the job he has to do. If he is to rise again, he must do so by establishing his *right* to a higher regard by virtue of his knowledge and his character. Is it not probable that a broader training in both the humanities and in the science of medicine, would help towards this desirable end?

In my desire to see the doctor of the future once more a highly educated man,† I shall be accused, I am sure, of a most impracticable idealism; but can we afford not to attempt this ideal? Standards of education and knowledge are rising everywhere and doctors must stay out in front where they belong.

Let me, however, add one practical suggestion. Ward work in hospitals has now reached a point where constant supervision by someone adequately trained in pathology and physiology is desirable throughout the 24 hours. Here is an opening for the employment of our students. Why should they not be added as auxiliaries to the resident staff of the Hospital? They could be apprenticed year by year to the hospital, if you like, and given at least their board and their lodging. What an improvement in pre- and post-operative techniques we should see, and what a remarkable training in applied medicine these students would receive. Most important of all, the prohibitive cost of a longer medical training would be partly met and the hopeless overcrowding of the purely clinical curriculum to a great extent solved. By their constant presence at the bedside these students would pick up, without much extra effort, the details of the more specialized techniques.

2. STANDARDS OF CONDUCT

Who am I to talk of ethics? Did Bernard Shaw not say that 'Every man is a rascal after 40'? At times I think we worry far too much about the minor peccadillos to which we are all prone. As a result we get bogged down in what Mr. Doolittle would call 'middle class morality'. Do we think the less of Samuel Pepys because, in addition to writing his *Diary* and reorganizing the Royal Navy, he yet found time to pleasure his wife's housemaid?

Looking beyond domestic felicities, we become aware of menacing clouds on the horizon. It is natural for a man with a scientific training to be attracted by the subjective view of ethics. It seems obvious to him that moral judgments are mainly rationalizations of the desires of the individual or of the society to which he belongs. I think most of you would subscribe to the view that 'the still small voice of conscience' is only the echo of early moral

* W. E. Wickenden, *The General Manager*.

* Since elevated to a life peerage.

† As exemplified by Francis Adam, a general practitioner of Banchory on Deeside, who, in 1853, was commissioned by the Sydenham Society to translate the *Corpus Hippocraticus*, and who refused the Chair of Greek at Aberdeen University, saying he could not leave his patients.

training. I would, however, ask those of you who hold this view to delve a little deeper. You will find that such an attitude does not bear philosophical analysis and, moreover, it carries with it such grave consequences that you must be very sure of your ground before you assert it; for this approach can be used to justify most of the gross political crimes of the last 50 years.

Political Hegemony

Some 40 years ago Germany withheld the knowledge of certain arsenicals from the rest of the world. She did this for political purposes, to embarrass those who were administrating her lost colonies. In the last War, the distribution of penicillin was handed over to a government department—I think it was the Department of Economic Warfare—a case of 'do as I ask, or you get no penicillin'. Those of you who served with the forces know only too well the aura of secrecy that surrounded such medical developments as DDT and BAL.

There is a real danger that medical advances and discoveries may be regarded primarily as belonging to the state, to be used or withheld according to political expediency. Sometime and somehow this attitude, so repugnant to our own doctrine that knowledge is international and must be held in common, will have to be fought. This will need the firm conviction that there is something unique in man's moral conscience and that his individual rights are inviolate.

Research and Ethics

During the war we were horrified by the experimental methods adopted by our German colleagues in prison camps. Are we also, to some extent, slipping in this matter in relation to clinical research?

Recently, in the British House of Commons, the Minister of Health was questioned about clinical experiments carried out in a British hospital without the knowledge and consent of the patients. He condemned such behaviour and, in answering, he referred his questioners to a relevant memorandum issued recently by the British Medical Research Council. That this Council had seen fit to issue such a memorandum seems to me tantamount to admitting that, at the very least, more care needs to be exercised.

Within the last few months, the holder of a professorial chair in Britain lauded the actions of those American parents who had offered their children as guinea-pigs for the trial of the Salk vaccine. Has a parent any such right? What if one of the unsafe vaccines had been used and some of these children had developed poliomyelitis. What would have been the reaction then? Are we returning to the days of Moloch?

It is fatally easy for the obsessional research worker to forget that the world is not contained in his laboratory. Perhaps all research programmes involving human beings should be approved in advance by an appropriate body. At least the same protection should be given to our patients as we afford to our other experimental animals.

Let me remind you of the story (apocryphal perhaps, but telling in its simplicity) of the Scottish professor turning away from the bedside, and saying to his class: *In corpore vili experimentum fiat*. And from the bed came the devastating reply: *Pro hoc corpore vilum Christus mortuus est*.

3. THE ORGANIZATION OF OUR PROFESSION

The Medical Association of South Africa

Of our Association I would say this: In trying to steer a safe course between the Scylla of trade unionism and the Charybdis of a medical society, it has by some miracle of seamanship piled itself up on both hazards. The Association was never designed as a trade union, indeed its Constitution forbids it to act as one. Whatever the legal niceties of the question, the basic function of trade unionism is collective bargaining. During the last 10 years we have been forced into such bargaining, however distasteful it may be to us.

The late Dr. Karl Bremer obviously expected us to act as a trade union when, at the annual dinner of our Branch in 1949, he said in reference to his projected scheme for the provision of medical aid on a national scale: 'I shall be buying wholesale, and I shall expect wholesale prices'.

We, I think mistakenly, have published such a list of prices in the *Tariff of Fees for Approved Medical Aid Societies*. Why this responsibility should have been accepted is one of the major mysteries of our organization. The rules within this list of fees are very close to trade union ideas. What can one think of Rule 7: '. . . once a medical practitioner has agreed to charge members at Medical Aid Societies tariff rates, he should charge such rates for all members of those Societies.'

Is this not going far beyond the normal activities of a medical association? I do not, however, decry these methods; indeed I am convinced that, faced by the modern state and modern industry, we need some such organization. However, our structure is quite unsuitable for any such function. You will recall that the British Medical Association could never make up its mind on this matter. For many years it held the General Practitioners, Union (a doctors' trade union affiliated to the Trade Union Congress) in disfavour. On the other hand, it established a Joint Standing Committee with the Trade Union Congress—a Committee which included on the Labour side such famous names as Ernest Bevin and Sir Walter Citrine; but the British Medical Association never came down on either side of the fence. What a different picture there might have been if, when the battle was joined over the State medical service, the medical negotiators had had the backing of responsible trade union opinion.

I do not advocate changing our Constitution; it is adequate for the duties of an old-style medical society, but it is not adequate for collective bargaining. We live in a different world from that of our fathers and grandfathers. However much we may dislike it, some form of contract practice (if only with the State) will continue to flourish, and we must be prepared for it.

If at present we cannot accept the idea of a full trade union, can we not form, in close conjunction with our present structure, a business organization or medical guild, capable of carrying out, at least, those functions of a trade union connected with collective bargaining?

How much pleasanter and how much more efficient it would be, if our Federal Council, having agreed on a policy, could say to those concerned: 'We should like to see this implemented, so now you must consult our business organization, which will deal with the financial considerations and terms of service.'

If past and present Federal Councillors find my suggestions iconoclastic and completely unacceptable, I would remind them of the appeal of Oliver Cromwell. No, not the notorious 'You have sat here overlong—in God's name, go'. I would not be so discourteous. Rather words more typical of the Lord Protector of England: 'I beseech you by the bowels of Christ, bethink ye that ye may be wrong'.

THE ARTIFICIAL KIDNEY IN THE TREATMENT OF RENAL DISEASE*

N. J. VAN RENSBURG, *South African Institute for Medical Research, Johannesburg*

After a brief description of the principles of diffusion, dialysis and osmotic pressure, on which the artificial kidney depends for its operation, and a description of one or two of the 127 models available in the USA, the various substances in the blood which must be dealt with were listed. By appropriate changes in the composition of the fluid surrounding the dialysing tubing of the apparatus, diffusion gradients are set up in such a way that substances in excess in the blood, e.g. urea or potassium, are removed, and ions such as sodium, chloride or bicarbonate, of which there may be a deficiency, can be restored to the blood.

The fact that the artificial kidney can only deal with some of the consequences of renal failure and cannot restore damaged kidney tissue was pointed out. The conditions for which the artificial kidney is valuable and those for which it cannot be expected to do good were detailed. The importance of correct clinical and chemical assessment in selecting patients who would benefit from the use of the artificial kidney and the difficulties

* Summary of a talk given at a Staff Meeting of the Institute on 13 April 1959.

involved in both acute and chronic renal failure were emphasized. In illustration several cases were described and discussed. Contra-indications to the use of the artificial kidney were pointed out.

At the conclusion of the lecture a plea was made for the artificial kidney to be used by a specialist team, including a physician, a cardiologist, and a biochemist, and that such teams should be few and located in heavily populated areas so that adequate experience and efficiency could be developed. Occasional use at long intervals would almost inevitably lead to poor results and bring a useful method of treatment into disrepute.

MEDICAL PRACTITIONERS OF UNKNOWN ADDRESS

The Registrar of the South African Medical and Dental Council has supplied the subjoined list of medical practitioners (with their present registered address) to whom communications addressed by the Registrar have been returned by the Post Office because delivery could not be effected. Attempts to trace these practitioners have failed. Their attention is invited to the following sections of the Medical, Dental and Pharmacy Act, 1928:

Section 16 (2). It shall be the duty of every registered person who changes his address to intimate the fact to the registrar within one month after such change.

Section 17 (1). The Council may erase from the register the name of any person who . . . (*b*) has failed, within a period of three months from the date of an enquiry sent by the registrar by registered letter to the address appearing on the register in respect of him, to notify the registrar of his present address.

Section 17 (3). No person whose name has been erased in accordance with this section . . . shall be deemed to be registered unless and until on application being made by him to the registrar, his name has been restored to the register.

N.B. In case the practitioners concerned do not see this notice friends who may know their present whereabouts are asked to advise them of the need to act immediately.

J. Carnegie, P.O. Kei Mouth, *via* East London.
M. B. Hodes, 1 Winchester Road, Mowbray, Cape.
P. G. M. G. Jones, c/o Dr. A. Wailer, N.B.S. Building, 20 Main Street, Port Elizabeth.
W. J. Kruger, Hospitaal, Middelburg, Transvaal.
L. Lambinon, 36 Navigation Road, Iscor Township, Pretoria.
D. R. Lee, c/o Barclays Bank, D.C.O., Oceanic House, 1 Cockspur Street, London, S.W. 1, England.
M. F. Mathews, c/o 11 Howard Centre, Pinelands, Cape.
R. J. S. Metz, 11 Tyrone Avenue, Parkview, Johannesburg.
D. J. C. Roberts, 53 Medical Centre, Field Street, Durban.
G. E. J. Seymore, Algemene Hospitaal, Pretoria.

THE COLLEGE OF PHYSICIANS, SURGEONS AND GYNAECOLOGISTS OF SOUTH AFRICA
DIE KOLLEGE VAN INTERNISTE, CHIRURGE EN GINEKOLOË VAN SUID-AFRIKA

The following candidates were successful in the examinations of the College held in Cape Town in May 1959:

Fellowship of the College of Surgeons of South Africa—Part I

Abramowitz, Israel
Engelbrecht, Jacobus Adriaan
Gampel, Basil
Louw, John Xavier
Mieny, Carel Johannes
Norman-Smith, Jack
Wilson, Paula Margaret

Fellowship of the College of Surgeons of South Africa—Part II

Marais, Johannes Stefanus

Diploma in Midwifery of the College of Obstetricians and Gynaecologists of South Africa

Phillips, Gerald Isaac
van Huyssteen, Hendrik Roelof

There were 21 candidates for the Part I examination for the Fellowship of the College of Surgeons, 2 for part II, and 7 for the Diploma in Midwifery.

PASSING EVENTS : IN DIE VERBYGAAN

Research Forum, University of Cape Town. A meeting of Research Forum will be held on Tuesday 2 June at 12 noon in the large A-floor lecture theatre, Groote Schuur Hospital, Observatory, Cape. Dr. M. Sacks (Department of Pathology) will speak on 'Aortic and coronary atherosclerosis in the 3 racial groups in Cape Town'. All who are interested are invited to attend this meeting.

* * *

Red Cross War Memorial Children's Hospital, Rondebosch, Cape The next meeting in the Postgraduate Seminar Series of lectures, held under the auspices of the University of Cape Town, Department of Child Health, will be held in the lecture theatre of this hospital on Wednesday 3 June at 5 p.m. Drs. H. Walton and S. Wolff, psychiatrists, will speak on 'The signs of the common behaviour disorders of childhood'. All practitioners are welcome.

* * *

South African Paediatric Association (M.A.S.A.). A meeting of the Cape Town Sub-group of this Association will be held on Tuesday 2 June in the lecture theatre, Red Cross War Memorial Children's Hospital, Rondebosch, Cape, at 8.15 p.m. Prof. J. H. Louw, who has recently returned from a visit to the USA and the UK, will speak on 'Impressions of paediatric surgery in the United Kingdom and the United States of America'. All practitioners are welcome.

* * *

Dr. Charles Keast, M.B., Ch.B., M.R.C.O.G., has commenced practice as a specialist gynaecologist and obstetrician at CNA Buildings, Oxford Street, East London. Telephones: Rooms 6900, residence 81234; if no reply 5515.

Dr. Charles Keast, M.B., Ch.B., M.R.C.O.G., het as spesialis-ginekoloog en verloskundige begin praktiseer te CNA-Gebou, Oxfordstraat, Oos-Londen. Telefone: Spreekkamer 6900, woning 81234; indien geen antwoord 5515.

* * *

Dr. A. Kessler, M.B., B.Ch., Dip. Surg. (Rand), has commenced practice as a specialist neurosurgeon at 218 Medical Centre, 110 Park Drive, Port Elizabeth. Telephones: Rooms 3-7190, residence 2-5515; if no reply 2-1545.

Dr. A. Kessler, M.B., B.Ch., Dip. Surg. (Rand), het as spesialis-neurochirurg begin praktiseer te Mediese Sentrum 218, Parkpad 110, Port Elizabeth. Telefone: Spreekkamer 3-7190, woning 2-5515; indien geen antwoord 2-1545.

* * *

'n Simposium oor voorgeboortelike versorging sal vanaf 1-6 Junie 1959 in Groningen en Rotterdam (Nederland) georganiseer word. Die onderwerpe van die Simposium is: ‚Suikersiekte en swangerskap', ‚Die funksie van die skildklier by swangerskap', ‚Oestriol uitskeiding gedurende swangerskap ('n hulp vir die berekening van die funksie van die plasenta)', ‚Sitologie gedurende swangerskap', ‚Byniere en swangerskap', en ‚Onvrugbaarheid'. Die Simposium sal bygewoon word deur verskeie wêreldberoemde vroueartse.

* * *

National General Practitioners' Group, Cape Western Sub-group. At the well attended Annual General Meeting of this Sub-group held on Wednesday 13 May at Medical House, Cape Town, the following office-bearers were elected for the ensuing year: Chairman, Dr. A. G. Paterson; Vice-chairman, Dr. F. E. Hofmeyr; Secretary/Treasurer, Dr. Norman Levy (210 Medical Centre, Heerengracht, Cape Town); Executive Committee, Drs.

C. H. Bösenberg, A. Gordon, R. Heald, S. R. Levy, S. Schur, C. Shapiro, J. Silberbauer, and I. Wolfsohn. The Sub-group wish to remind all general practitioners that if they have any problem, they are invited to contact the Secretary or any member of the Committee.

Nasionale Algemene Praktisynsgroep, Wes-Kaaplandse Subgroep. Die volgende ampsdraers is gekies vir die jaar wat voorlê op die Jaarlikse Algemene Vergadering van hierdie Subgroep, wat goed bygewoon is, op Woensdag 13 Mei te Mediese Huis, Kaapstad: Voorsitter, dr. A. G. Paterson; Vise-voorsitter, dr. F. E. Hofmeyr; Sekretaris/Tesourier, dr. Norman Levy (Mediese Sentrum 210, Heerengracht, Kaapstad); Uitvoerende Komitee, drs. C. H. Bösenberg, A. Gordon, R. Heald, S. R. Levy, S. Schur, C. Shapiro, J. Silberbauer en I. Wolfsohn. Die Subgroep wil alle algemene praktisyns graag daaraan herinner dat hulle versoek word om met die Sekretaris of met enige lid van die Komitee in verbinding te tree oor enige probleem wat mag voorkom.

NEW PREPARATIONS AND APPLIANCES : NUWE PREPARATE EN TOESTELLE

GRISOVIN TABLETS

Glaxo Laboratories (S.A.) (Pty.) Ltd. wish to announce that Grisovin tablets are now available in bottles of 25 tablets as well as in bottles of 100 and 1,000 tablets as announced in this Column on 9 May (**33**, 405).

HIGH-PROTEIN BABY CEREAL

Hind Bros. & Co. Ltd., in introducing Hinds Protein Baby Cereal, supply the following information:

The need for a high-protein cereal has been met by Hind Bros., who have introduced this new variety to their existing range of cereals.

Hinds High-Protein Baby Cereal contains malt extract, sorghum (Mabela), oatmeal, wheatmeal, soya-bean meal, skimmed milk solids, calcium carbonate, sucrose, extra B vitamins, and additional protein.

Further details may be obtained from Hind Bros. & Co. Ltd., P.O. Box 2823, Durban.

CORTUCID EYE-DROP CREAM

Westdene Products (Pty.) Ltd. announce that Cortucid, manufactured by British Schering, of London, is now available, and supply the following information:

Cortucid is a bland, fluid cream containing the powerful anti-inflammatory agent hydrocortisone together with sulphacetamide, the bacteriostat of choice for ocular therapy.

Cortucid ensures prompt relief of inflammatory eye conditions whilst protecting the eye against the increased risk of infection associated with the use of hydrocortisone.

Cortucid is of particular value in the treatment of eye conditions in which inflammation is an important factor, whether this be of bacterial, allergic, or of traumatic origin.

Cortucid is presented as a water-miscible, fluid cream which drops readily from the tube and liquefies immediately on contact with the conjunctiva. Since the nozzle does not touch the eye contamination of the contents of the tube is avoided.

Cortucid is available in 3 g. tubes.

Samples and further information may be obtained from the sole South African distributors, Westdene Products (Pty.) Ltd., P.O. Box 7710, Johannesburg, and their branches.

NEO-MERCAZOLE

Westdene Products (Pty.) Ltd. announce that Neo-mercazole, manufactured by British Schering, of London, is now available, and supply the following information:

Since Neo-mercazole was first introduced it has steadily superseded earlier anti-thyroid drugs because of its high therapeutic potency and its greater freedom from toxic side-effects. It is now widely accepted as the anti-thyroid drug of choice.

As Neo-mercazole does not make the thyroid gland hard, friable or vascular, and consequently difficult to operate on, it is also the ideal drug for rendering patients euthyroid before surgery.

Neo-mercazole is tasteless and has the added advantage that patients are not required to swallow a large number of tablets each day.

Neo-mercazole is available as tablets, each containing 5 mg. of carbimazole, and supplied in containers of 100 and 500 tablets.

Samples and further information may be obtained from the sole South African distributors, Westdene Products (Pty.) Ltd., P.O. Box 7710, Johannesburg and their branches.

OBLIVON-C

Westdene Products (Pty.) Ltd. announce that Oblivon-C, manufactured by British Schering, of London, is now available and supply the following information:

Oblivon-C is a particularly safe drug which has proved very effective in the treatment of those conditions in which anxiety is the dominant factor. In the day-to-day management of anxiety states, anxiety neuroses, phobic conditions, functional and psychosomatic disorders, Oblivon-C effectively relieves the stress factor in these cases by its specific action on anxiety.

Oblivon-C is the most suitable tranquillizer for use in general practice because of its reliable action and its freedom from side-effects. There are no contra-indications to its use.

Oblivon-C is available in the form of oval tablets specially shaped to make them easy to swallow, and is supplied in containers of 25 and 100 ovets. Each ovet contains 100 mg. of Oblivon-C (methylpentynol carbamate).

Oblivon elixir is a shorter-acting tranquillizer than Oblivon-C. Oblivon elixir rapidly allays fear and reduces tension before minor medical and surgical procedures. It plays an important role in dentistry and pre-anaesthetic medication. The elixir is presented as a palatable liquid in bottles of 100 ml. and is particularly suitable for children and old people.

Samples and further information may be obtained from the sole South African distributors, Westdene Products (Pty.) Ltd., P.O. Box 7710, Johannesburg, and their branches.

SECROSTERON

British Drug Houses (South Africa) (Pty.) Ltd. announce the introduction of Secrosteron, a new fundamental discovery from the research laboratories of British Drug Houses Ltd., London.

Secrosteron is a new synthetic, orally active, purely progestational substance which has been shown to be approximately 12 times as potent as ethisterone in biological studies. Because of the absence of side-effects, Secrosteron can be given in higher doses than other progestational agents, and preliminary studies indicate that the new substance produces a better and more uniform response in which growth of glandular tissue as well as growth of stromal tissue takes place. Secrosteron has no androgenic, oestrogenic or anabolic activity.

Composition. Each Secrosteron tablet contains 5 mg. of 6 : 21-dimethyl-ethisterone which has been given the approved name of dimethisterone.

Indications. Secrosteron is indicated in the treatment of habitual and threatened abortion, secondary amenorrhoea, premenstrual tension, menorrhagia, sterility (due to endometrial dysfunction), and metrorrhagia.

Administration and dosage. Secrosteron is given orally. For dosage schedules detailed literature is available on request.

Packing. Bottles of 30 and 100 tablets.

BOOK REVIEWS : BOEKBESPREKINGS

RADIOLOGICAL ATLAS

Atlas de Radiologie Clinique de La Presse Médicale. (Série la 100 1953-58.) 1,764 figures. Paris: Masson et Cie. 1958.

This publication consists of 100 separate sections, each a 4-page loose-leaf illustrated article, dealing with a particular aspect of diagnostic radiology. Of these articles the first ½-page at most is devoted to text and the remaining 3 pages to excellently repro-

duced radiographs. Since each page is of 14 by 10 inches dimensions it is possible to reproduce a very large number of radiographs; altogether there are no less than 1,764 figures.

Most aspects of diagnostic radiology are covered. There are sections devoted to the heart, genito-urinary system, bones, skull (including angiography), lungs and the gastro-intestinal system.

This atlas represents the fruits of many labourers gathered during the years 1953-58. Of the many contributors all are French. The text is in French. The radiographs, however, are of such good quality that to radiologists and those interested in diagnostic radiology the accompanying legends are hardly of importance and the language problem is therefore almost non-existent. This publication is, therefore, recommended for inclusion in radiological libraries.

W.J.L.

DERMATOLOGY AND SYPHILOLOGY

The Year Book of Dermatology and Syphilology—1957-58. Edited by Rudolf L. Baer, M.D. and Victor H. Witten, M.D. Pp. 492. 64 figures. 88.00. Chicago: Year Book Publishers, Inc. 1958.

As most dermatologists consider the Year Book an essential purchase representing the best available abstract service in the English language there is little for the reviewer to say. This year's editorial article is concerned with test procedures in allergic contact dermatitis. The practical applications are considered in greater detail than in any other single article that one can recall and there are few who will not find some useful suggestions for the improvement of their technique. The abstracts are, as always, well done and the editors' comments pertinent. Roughly 50% of the articles abstracted originated in the United States; this is a change for the better compared with 1950, when the percentage was 66, and if the trend persists the Year Book may really become international in its scope.

J.M.

UROLOGY

The Year Book of Urology—1957-58. Edited by William Wallace Scott, M.D., Ph.D. Pp. 359. 79 figures. $7.50. Chicago: Year Book Publishers, Inc. 1958.

The present Year Book, under the editorship of William Wallace Scott, has maintained the extremely high standard, which the Editor has previously set.

The editorial is of particular interest to the urologist. The Editor presents his own views regarding the study of disseminated prostatic cancer and its management by hormonal therapy. Professor Scott is an authority on this subject, and in this article asks some very pertinent questions, which it will pay the research-inclined urologist to examine, digest and, if possible, act upon.

Thereafter we are given to consider the numerous branches of urological medicine, under well-defined headings, and also several branches of medicine which are allied to urology or in which the urologist occasionally has to trespass.

All the articles summarized are concise in their subject matter, and are therefore a very useful adjunct to the library of the urologist. The articles are well summarized, but to this reviewer the pertinent, and often witty, comments made by the Editor remain a source of great pleasure and instruction.

If the reviewer were allowed to offer a minor criticism of an otherwise excellent presentation, it would be that the genitalia should be subdivided into male and female genitalia, and that more prominence should be given to the numerous rather vexing female urological problems with which the urologist is often required to deal. It seems that the necessary accentuation of the numerous female complaints with which the urologist is presented has been sadly neglected by the urological fraternity over many years.

J.N. de K.

INTERFERENCE MICROSCOPE

The Interference Microscope in Biological Research. By Arthur J. Hale, M.B., Ch.B., Ph.D. Pp. xi+114. 95 figures. 20s. net + 1s. 4d. postage abroad. Edinburgh and London: E. & S. Livingstone Ltd. 1958.

The interference microscope was first introduced in 1894 but it did not become a practical instrument until the late 1940s, soon after which it was shown that it could be used to measure the total amount of material in a tissue, cell or cell component.

The purpose of this book as stated in the author's preface is to describe the basic phenomenon involved, the designs of the instruments which have been introduced, and the theoretical basis of the measurements of mass, thickness and concentrations of materials in very small objects. The use of the commercially available instruments and the errors and limitations of the method are also discussed.

The interference microscope can be used merely for the examination of cell morphology, but the main value of the technique is that it permits the quantitative measurements mentioned above. Used alone, or in conjunction with other methods such as microspectrophotometry and general cytochemical techniques, it must play an important roll in the elucidation of problems of cell metabolism.

The biologist concerned with the investigation of these cellular processes will welcome the appearance of this book, which will help him to become familiar with the principles underlying the method he will be using.

T.G.S.

HAEMATOLOGY

Laboratory Medicine—Hematology. By John B. Miale, M.D. Pp. 735. 192 illustrations. 9 plates, including 5 in colour. South African price: £5 17s. 0d. St. Louis: The C. V. Mosby Company. 1958.

This book provides an excellent outline of haematology and will enable the student of haematology, the clinician, haematologist and technologist to get an easily readable description and a clear insight into the various facets of haematology. A full list of references is given at the end of each chapter.

The illustrations of blood and bone-marrow cells (normal and abnormal) are helpful and have been reproduced in colour (Wright's stain). Nuclear detail is not as clear as it might have been, but this is not easily reproducible in text-books.

Cases of the various conditions (megaloblastic anaemias, leukaemias etc.) are presented, with clinical and laboratory data, discussion, and illustrations in black-and-white. These aptly serve to emphasize the cooperation that should exist between the laboratory and the clinician.

The chapters on blood transfusion, haemostasis and blood coagulation, deficiency anaemias, aplastic anaemias and the myeloproliferative syndromes, and leukocytes and diseases of leukopoiesis are well presented and provide a good understanding of each subject. There is an excellent up-to-date summary of the haemolytic anaemias.

Laboratory methods are given in an appendix at the end of the book.

In general this is a most useful addition to the haematology library.

S.J.R.

THE SCIENTIFIC BASIS OF MEDICINE

British Postgraduate Medical Federation, University of London. Lectures on the Scientific Basis of Medicine. Volume VI. 1956-57. Pp. ix+393. Illustrations. 45s. net. London: University of London, The Athlone Press. 1958.

This is the 6th annual volume of lectures in the series arranged by the British Postgraduate Medical Federation. They were given in the winter of 1956-57. Like their predecessors the speakers were selected for their eminence in the profession and their wide knowledge, and in most cases intimate experience, of the subjects which they were invited to discuss. The bibliographies at the end of the lectures vividly illustrate the large number of original papers which many of the authors have themselves contributed.

The lectures included in this volume cover a wide range of subjects. As befits this age, biochemistry receives considerable attention and, while there is often mention of the relevance of the topic to clinical medicine, one might well be a little lost if one's biochemistry has become rusty. But just as we can pick and choose the lectures we attend so we can select or reject the ones we choose to read. There are a few more clinically orientated, but one cannot but regret the omission of Sir Russell Brock's lecture on 'The relationship between the embryology and morphology of the heart and cardiac surgery' and Paul Woods' on 'The physiological basis of clinical signs in heart disease'—both of which were delivered in this series.

The book contains lectures on viruses and other organisms, endocrinology and psychiatry, atomic energy and biological systems—and many more, for there are 21 lectures in all. They reflect new techniques and trends of modern research. The book is authoritative and up to date and there are few of us who would not find something of interest in its pages.

C.M.

NEOMYCIN

Neomycin. Its nature and practical application. Edited by Selman A. Waksman. Pp. x+412. 41 figures. 40s. London: Baillière, Tindall and Cox Ltd. 1958.

The research on antibiotics has been so intensive, extensive and productive that monographs on individual agents have become necessary in medical literature. This volume dealing with the neomycin complex is a model that should be carefully studied by future authors. It is written by experts, including the discoverer of this broad-spectrum antibiotic (Waksman), who also discovered the streptomycin complex. There is great detail on the discovery, the production, and the antimicrobial, pharmacological and therapeutic properties of this widely used antibiotic still hardly 10 years old. The information is well presented, extensively documented and illustrated, and should serve not only as an account of neomycin but as an example in the presentation of knowledge on antibiotics in general.

Neomycin has found an important place in human and animal therapy. It is not the only antibiotic produced by *S. fradiae*, which is fast becoming an organism of distinction, but it is being extensively used as the most important antibacterial agent in intestinal antisepsis, in certain enteric infections (including diarrhoea due to enteropathogenic *E. coli*), and as the drug of choice for intraperitoneal administration and for many infections by local application on skin and mucous membranes. The book is a 'must' for microbiologists, pharmacologists, physicians, veterinarians, and manufacturers of antibiotic preparations.

N.S.

TUMOURS OF THE MOUTH AND JAWS

Histopathologie der Tumoren der Kiefer und der Mundhöhle. Von Prof. Dr. E. Langer. vii+167 Seiten. 212 Abbildungen. DM 49.50. Stuttgart: George Thieme Verlag. 1958.

The author describes very thoroughly the tumours of the jaws, the salivary glands and the oral cavity. He deals with anatomical aspects and some clinical findings. The descriptions are rather short, but there are many good illustrations (they should not be retouched) demonstrating the neoplastic structures. Since the author wrote this book for surgeons, dentists and dentistry students, the reviewer may make the following two remarks. The forms of naevi pigmentosi are so important for the prognosis that the author should have explained the differentiation of junctional and intradermal naevi. And although the author does not agree with the opinion that the giant-cell epulis is no true neoplasm he should have mentioned the findings which suggest that the giant-cell epulis is a reactive process. But on the whole Langer's book gives a good review of the tumours in the jaws, the oral cavity and the salivary glands.

H.W.W.

CORRESPONDENCE : BRIEWERUBRIEK

REMUNERATION OF PART-TIME MEDICAL OFFICERS

To the Editor: In the *Journal* of 25 April (**33**, xxvi) an advertisement for a part-time medical officer required by the City Council of Germiston, is published. Apart from the fact that the advertisement does not state what I know to be a fact—that this part-time medical officer will be required to be on call 24 hours a day and 7 days a week for emergencies, let us consider the salary at its face value:

£43 17s. 6d. per month is offered for 6 3-hour sessions a week. Taking the month of May as an example, 26 sessions, or 78 hours of duty will be required at a remuneration of just over 11s. an hour. No increments. No pension fund. No additional remuneration for overtime.

Does the Association approve of this state of affairs? If not, does the Association consider this salary derogatory to the medical profession—in which case any applicant will be contravening an established and accepted ethical rule.

Jack

29 April 1959

DIE KUX-OPERASIE

Aan die Redakteur: Ek het al lankal gewonder hoe dat 'n medikus hom *so* kan laat beduiwel om liries te raak oor die Kux-operasie. Nou verstaan ek dit, na die lees van die brief uit Pietersburg waarin onder andere gemeld word van die ‚dramatiese sielkundige verandering' wat die pasiënte na die operasie sou ondergaan, want die Kuxiste (moenie verwar word met koesisters nie) beweer dat hulle self die operasie ondergaan het. Nou word die saak vir my mos duidelik—'n medikus moet eers sielkundig gekondisioneer word om sy jare van wetenskaplike opleiding te ignoreer.

En wat die aanmerking betref, ‚ons resultate is *so* belowend dat ons voel dat hierdie ingreep waarskynlik 'n permanente plek in medisyne sal inneem', wil ek hulle troos: Wees maar gerus. Die Kux-operasie *sal* 'n permanente plek inneem, nl. op die boonste rak van 'n mediese museum van rariteite.

R.S.V.

12 Mei 1959

TAALRUBRIEK

Aan die Redakteur: Die Taalkomitee van die Fakulteit van Geneeskunde van die Universiteit van Stellenbosch moet geluk gewens word met hulle grootse poging om Afrikaans as mediese taal op 'n verstandige wyse te wysig.

Veral is dit verblydend dat hulle die bestaan van so iets as 'n kogleêre uterus (cochleate uterus) erken. Onlangs het 'n wêreldberoemde verloskundige en ginekoloog van Amerika in Kaapstad op 'n vraag wat ek hom gestel het, erken dat hy nie weet wat 'n kogleêre uterus is nie; nog minder het hy geweet wat die behandeling vir die lastige simptome van dié entiteit is.

Ek is gereed om aan die mediese personele van die Universiteit van Kaapstad en van die Universiteit van Stellenbosch eens en vir altyd te demonstreer dat die entiteit wel bestaan, en om die metode van behandeling wat met 100% goeie resultate toegepas kan word, aan te toon.

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11 Mei 1959

CORONARY ARTERIES OF THE BANTU HEART

To the Editor: A few comments in Professor Brink's letter[1] require objective discussion:

1. The apologia for his earlier conclusions,[2] as stated in the two opening and third last paragraphs of his letter, are quite unnecessary, for in the introductory sentences of my paper[3] I clearly acknowledged the tentative nature of his studies as follows: 'Since the publication of Brink's *preliminary report*[4] in 1949 . . . the above facts have, *at times*, been attributed to a racial morphological difference in the coronary artery distribution . . . ' (my italics).

2. *Techniques.* Research workers agree that techniques, generally speaking, are merely a means to an end. A technique may be subject to modification, depending upon the circumstances and requirements. Certain techniques require scrupulous adherence especially *if one is actually checking the technique itself*, but where the technique is merely one of several methods of obtaining results, the choice rests with the investigator.

As I have constantly quoted observations from Schlesinger's paper,[5] I was fully aware of his technique and of his views on dissecting methods as quoted by Professor Brink. Unfortunately, Professor Brink's quotation is out of context and therefore may tend to be misinterpreted by readers. Schlesinger also stated: 'A new technique was devised, because all previously available

methods proved inadequate *for visualizing the entire coronary artery tree simultaneously*' (my italics), and later, 'Based on the data thus acquired, description of the development, distribution and significance of the *compensatory anastomotic circulation connecting the various branches of the coronary artery* system has been published elsewhere . . . ' (my italics). My paper makes no pretence of performing such a complicated survey of anastomoses of small extra- and intra-mural vessels for which Schlesinger's technique (which in itself is a modification of that of Gross[6]) is ideal. In fact, I specifically indicated the restricted limits of my survey, for at the end of the fourth paragraph of my paper I clearly stated: 'In the present paper the left coronary artery (A. coronaria sinistra) and its branches will be chiefly considered.' As this vessel and the branches under consideration are large and superficial, nothing more than simply stripping away the fat and visceral pericardium was necessary to demonstrate them clearly. This procedure is adequate and suitable even for second-year medical students. Consequently, Professor Brink's reference to 'incompletely and carelessly performed dissection', 'inadequate approach', etc. are entirely uncalled for and introduce a derogatory and personal note which is undignified, to say the least, in a scientific discussion between colleagues. If Professor Brink 'was therefore glad to hear that others had taken up the matter' (i.e. of studying the coronary artery distribution in the Bantu heart), it appears illogical that he should react so violently to criticism of his preliminary observations of which he admits that only 'a pattern may have been described'.

3. *The 'third primary division'*. Professor Brink persists in stating, despite his acknowledgment of the preliminary nature of his investigation of a statistically insignificant (17 European, 15 Bantu, and 1 Coloured) group, that 'on the basis of careful investigation, I believe it to be an *additional* branch over and above branches 12 and 14 of Spalteholz'. My paper, based on 278 hearts, clearly proves that this 'third primary division' *cannot* possibly be an additional branch, but is merely an individual variation in position of origin of 'branches 12 or 14', irrespective of race or sex.

Professor Brink further states that 'Dr. Singer, for unknown reasons, wishes to rename these latter branches' (i.e. branches 12 and 14). I prefaced my observations by stating that the Spalteholz classification is neither satisfactory nor in current usage, and an extensive paragraph was devoted to explain that this classification is very confusing. I introduced alternative terms to indicate functional distribution (which also appeared more logical to anatomical colleagues overseas) so as to make confusion less confounded. So, why 'unknown reasons'?

Professor Brink states in his letter 'that the third primary division was a replacement of branches 12 or 14 was recognized by me . . . ' In actual fact, in his original report, this recognition is not stated anywhere, and in every illustration therein where the 'third primary division' is drawn, branches 12 and 14 are also present. Furthermore, the legends to his illustrations of both Bantu and European hearts actually unwittingly *support* my contentions.

Professor Brink states in his preliminary report: 'The most significant finding is the high incidence of a third primary division in the Bantu heart'. The contention of my paper is that the occurrence of this vessel is not significant in the Bantu, occurring almost equally in Bantu, White and Coloured as an individual variation.

4. *High-terminating anterior descending branch of the left coronary artery*. My paper reads: 'In this regard Brink does not define metrically what is meant by "normal", "high" or "low" termination'. I also stated 'there is no constant correlation between the origin of the major or minor LVA at the bifurcation and the distance travelled by the anterior interventricular artery'. I cannot quite understand Professor Brink's 'astonishment', as I had commented on the distance travelled by the major LVA, not whether the anterior interventricular artery turns round the apex of the heart and runs backwards for a variable distance in the posterior interventricular groove, which it *usually does* irrespective of race. I admit that I did not state the case very dogmatically, but I did not think it was necessary to comment on his observation of what is accepted as a normal variation' and which he correctly noted in a variable number of cases. However, it follows clearly from my remarks (*vide supra*) that when a large minor LVA supplies the anterior surface of the left ventricle the major LVA is small or short, and, *pari passu* the anterior interventricular artery then 'conserves' its distribution for the posterior aspect of the heart (i.e. as a so-called 'high' terminating anterior descending branch of the left coronary artery).

What should 'astonish' Professor Brink is not my 'failure to have grasped the meaning of a high terminating anterior descending branch', but my tactful consideration in not having stated that he had observed what is generally recognized in the standard text-books as a common variation. In actual fact I comprehend only too well 'the significance of a longer branch which could act as a greater source of collateral supply'.

5. *Right coronary preponderance*. Unfortunately Professor Brink, in his letter, again misinterprets Schlesinger's view. In defining the term from his observations on a particular heart, Schlesinger states ' . . . . *the right coronary artery supplies blood to a large part of the posterior wall of the left ventricle*. In addition, from it arises the posterior descending coronary artery. This heart is a right coronary artery-preponderant heart because this artery supplies all of the right ventricle plus the posterior half of the interventricular septum plus part of the left ventricle' (my italics). What justification is there, then, for Professor Brink to criticize my interpretation as follows: 'The statement that Schlesinger meant that the right coronary artery also supplies part of the left ventricular wall posteriorly in the region of the septum, is therefore incorrect'? If Professor Brink is not convinced by my anatomical observations, may I once again quote from Gray's *Anatomy* where it states in relation to the distribution of the right coronary artery: ' . . . near its termination it gives off a *posterior ventricular branch*, which runs forwards in the posterior interventricular groove, supplies branches to both ventricles and anastomoses near the apex of the heart with the anterior interventricular branch of the left coronary artery'. May I be permitted to point out to Professor Brink that the posterior ventricular branch is synonymous with the posterior descending branch of Schlesinger, and that only when it and the right coronary increase their distribution to that part of the left ventricle usually supplied by the ramus circumflexus of the left coronary artery, is the term 'right coronary preponderance' applicable. This is clearly stated in the above quotation from Schlesinger, who obviously used the term 'right coronary artery-preponderance', and not 'posterior descending artery-preponderance', because, in these cases, the increased distribution of the posterior interventricular artery is only part of the picture. However, the important point is that right coronary preponderance appears (as an individual variation) as a relatively constant ratio in a number of racial groups, as indicated in my paper, and with which Professor Brink now half-heartedly agrees.

Professor Brink now states: 'However, right preponderance was not claimed as a particular feature of the Bantu heart', yet in his 1949 report he categorically affirms 'on this evidence it appears that there is a significantly different coronary artery pattern in the Bantu hearts studied, namely a third primary division, high terminating anterior descending branch of left coronary and right coronary preponderance. The European hearts in contrast showed no uniform pattern'.

I wholeheartedly agree with Professor Brink that 'the presence of emotive phrases together with erroneous comparisons, and the failure to study all the aspects of the problem' is highly undesirable, but beyond that I do not consider it necessary to comment on his views of my publication which appeared in a highly reputable medical journal.

Finally, in view of the above discussion there is no necessity to correct my statements, as suggested by Professor Brink. Furthermore, I am now even more convinced that a specific pattern has not been described for the coronary artery distribution in the Bantu heart.

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1. Correspondence (1959): S. Afr. Med. J., 33, 407.
2. Brink, A. J. (1949): Clin. Proc., 8, 137.
3. Singer, R. (1959): S. Afr. Med. J., 33, 310.
4. Brink, A. J. (1949): Clin. Proc., 8, 137.
5. Schlesinger, A. J. (1940): Arch. Path., 30, 403.
6. Gross, L. (1921): *The Blood Supply of the Heart*. London: H. Frowde and Hodder and Stoughton.
7. Johnston, T. B., Davies, D. V. and Davies, F., in Gray, H. (1958): *Anatomy*. London: Longman, Green and Co.